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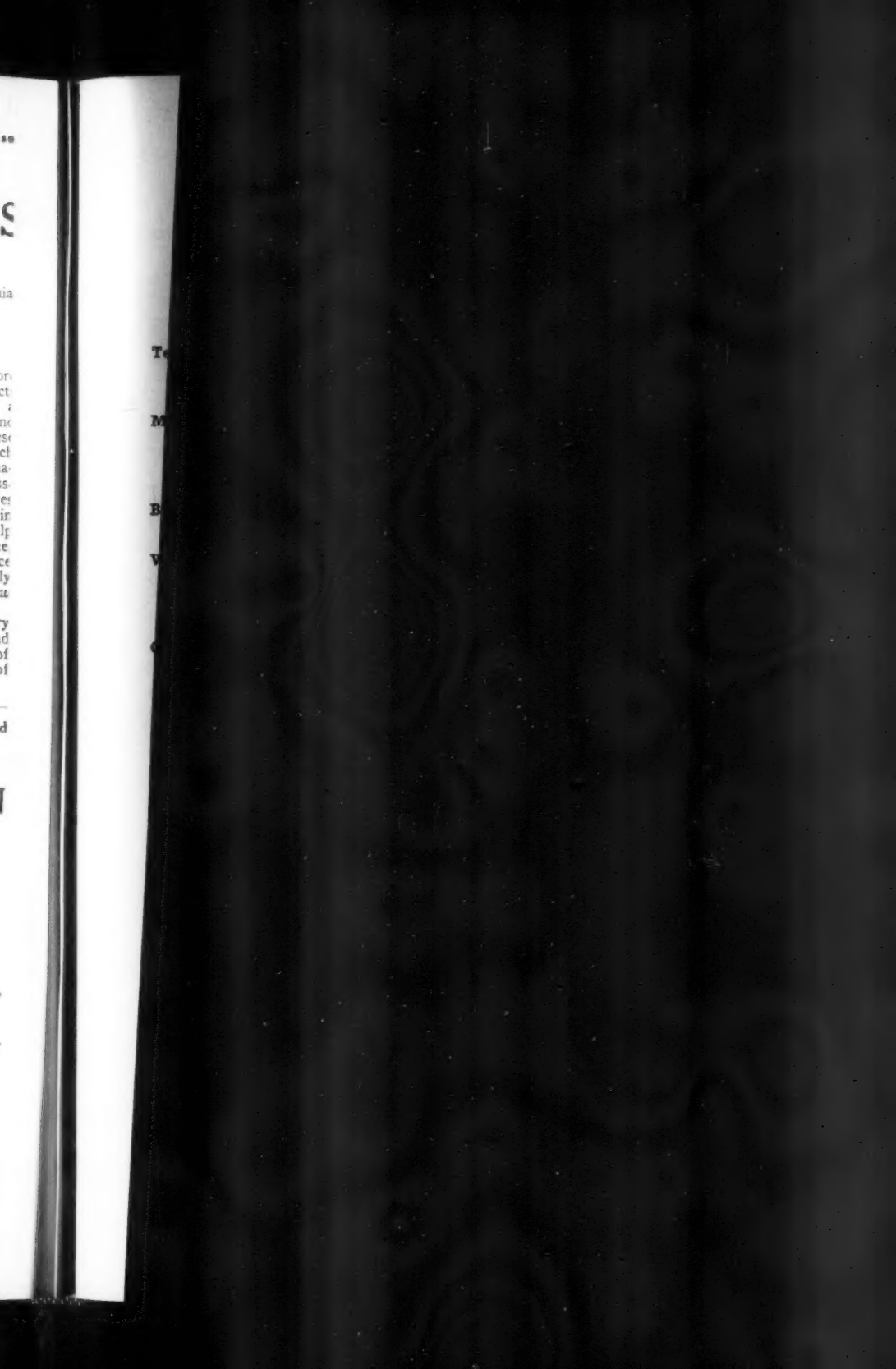

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

NOVEMBER, 1912

ORIGINAL ARTICLES

TERTIARY SYPHILIS OF THE LIVER.[1]

By Thomas McCrae, M.D., F.R.C.P. (Lond.)

PROFESSOR OF MEDICINE IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

(From the Medical Clinic of the Johns Hopkins Hospital.)

There is a peculiar importance attached to the recognition of late syphilis in that diagnosis may mean and determine the issue between life and death. This is most strikingly shown in the tertiary lesions of the nervous system, but it also applies to syphilis of the liver. The symptoms caused by it are often serious and without diagnosis the issue may be fatal, whereas with its recognition and proper treatment we have in the majority of cases a demonstration of one of the most brilliant results of therapy. It is the recognition which is so important and therefore the clinical features are especially considered in this paper.

The study is based on 56 cases which were admitted to the medical service of the Johns Hopkins Hospital. The cases of early congenital syphilis are not included; they form a group well recognized and are not considered here. The cases regarded as late congenital syphilis are included.

The incidence of tertiary hepatic syphilis is difficult to state with any accuracy. These 56 cases occurred among 27,500 general medical cases, and it does not seem unlikely that an unknown number were overlooked. Among 3300 autopsies at the Johns Hopkins Hospital there were 46 of well marked syphilis of the liver,

[1] Read before the Association of American Physicians, May 14, 1912.

but in many of these there were no clinical manifestations. Rolleston[2] quotes 64 cases among 11,629 autopsies at St. George's Hospital, London, and Flexner[3] 88 cases among 5088 autopsies at the Philadelphia Hospital. It is probable that the condition is more common than is generally recognized.

Etiology. The essential etiological factor does not require discussion. The contributing factors were as follows:

Age. The distribution by decades was:

1 to 10	1
11 to 20	2
21 to 30	11
31 to 40	19
41 to 50	16
51 to 60	4
61 to 70	3

The 3 cases below the age of twenty years were regarded as instances of late congenital lues. The age of onset in these was three years, thirteen years, and sixteen years. The oldest patient in the series was aged seventy years.

Color. Of the series, 34 were white and 22 colored. This shows an unusually high percentage among the colored patients, the ratio being 1.8 to 1, whereas in the medical service of the hospital the figures are about 5 to 1.

Sex. This shows a preponderance of males, there being 41 males and 15 females. The number of colored females is striking, 10 out of the 15 females being colored. There were only 12 colored males. The explanation of the incidence in males may lie in the greater prevalence of syphilis, although this may not apply in the colored race, but it is of interest to inquire the effect of over-indulgence in alcohol.

Alcohol. The three patients below the age of twenty can be excluded. Of the cases in which there was a definite note as to alcohol, in only 4 was there no history of drinking. Of 37 with a definite history, in only 3 was the record of slight use; 19 described themselves as moderate users, and 14 had taken it to excess. This is rather striking and shows a very high percentage of moderate or heavy users of alcohol. It may be a factor in determining the occurrence of hepatic syphilis, not, however, meaning by this that syphilis is engrafted upon alcoholic cirrhosis.

History of Syphilis. In the 3 congenital cases, there was a positive history of syphilis in the father of one; in the other two the history was very suggestive, as both mothers had had several miscarriages. In the adults there was a definite history of a primary infection in 26. In 9 others syphilis was suggested by a history of iritis, sore throat associated with eruption, miscarriages, etc. The time which had elapsed since the primary sore in the cases

[2] Diseases of the Liver, 1905.

[3] New York Med. Jour., 1902, p. 10.

with a positive history varied from four to twenty-five years. There were 3 cases with an interval of four years and 3 with five years. With an interval of from six to ten years inclusive there were 7 cases, from eleven to fifteen years 8 cases, from sixteen to twenty years 3 cases, and from twenty-one to twenty-five years 2 cases.

Morbid Anatomy. There were 46 cases among 3300 autopsies. The changes may be classified as cirrhosis, cicatrices, and gummata. Naturally there are various combinations of these. Of these 46 cases, in 23 there were changes described as cirrhotic; 19 showed cicatrices, and 21 gummata. In 8 cases there was a combination of gummata and cirrhosis, in 5 gummata and cicatrices, in 1 cicatrices and cirrhosis, and in 1 all three were present. In only 4 was amyloid change found. In 9 cases there were signs of syphilis found in other organs than the liver. In almost all the cases which came to autopsy the diagnosis was not made during life, the prominent features being due to disease elsewhere. In some a diagnosis was not possible, as there were no symptoms from and no signs of hepatic disease. Old scars in the liver cannot be recognized during life except in rare cases. The cause of death was very various, thus 14 died of cardiac and renal disease, 6 of pneumonia, 3 of acute peritonitis, 3 of tuberculosis, 2 of carcinoma, 2 of aneurysm, 2 of cerebral syphilis, and one each of gangrene, eclampsia, meningitis, accident, leukemia, etc.

Complaint. The study of the complaint made by the patient is of interest as showing the diversity of the symptoms for which relief was sought. Many of the patients had lesions other than in the liver. The most common was swelling of the abdomen, in 27 cases. Next in frequency was abdominal pain, usually referred to the upper abdomen, in 18 cases. Jaundice was the complaint in 7, shortness of breath in 5, loss of weight and strength in 3, vomiting in 2, fever in 2, and chills and fever in 3. In certain cases complaint was made of several of these conditions.

Previous History. The features which stand out prominently among the general symptoms are as follows: *Loss of weight* was the most frequent and had been more or less marked in 33 cases. The loss varied from fifteen to fifty pounds. Shortness of breath was marked in 10 cases and loss of strength in 9. Seven of the patients had suffered from fever, in 4 associated with chills. Two of the patients with chills and fever had been thought to have malarial fever, and had taken large doses of quinine over long periods. In one case there had been chills and fever over a period of eighteen months. In several of the others a diagnosis of tuberculosis had been made, apparently based largely on the occurrence of fever without any obvious explaining cause. Three patients suffered from severe sweating not associated with chills or fever. Swelling of the legs was marked in 8, but in all was associated with ascites.

Features suggesting disturbance in the abdomen were common. Of these the most frequent was swelling, which occurred in 34 cases, and next abdominal pain in 28 cases. Indefinite gastric disturbance was a feature in 14 cases and vomiting in 14 cases; in 7 of these there had been hematemesis and in 2 melena. In several of the cases the hemorrhage from the stomach had been very severe. Diarrhea was marked in 3 cases. Jaundice occurred in 17 cases, in some being so intense that there was a greenish tint to the skin.

The duration of the symptoms when the patient came under observation varied from one month to eleven years. The duration was three months or less in 13 cases, three to six months in 11 cases, between six months and one year in 2, from one year to a year and a half in 14, about two years in 7, three years in 4, and eleven years in one. In the others the history was uncertain. In the longer periods the severity of the symptoms was not constant; there were times of improvement and remission.

Previous Ascites. This is of particular interest in regard to the general question of cirrhosis of the liver and its prognosis. Seven of the patients had previous attacks of ascites which had required tapping and after which there had been marked improvement so that they gave up treatment. In 3 patients, 2 of whom had been tapped four times, the intervening period was under a year. In 3 patients the interval had been about a year, the number of tappings being one, two, and seven. The remaining patient had been tapped eleven times eleven years before and 86½ liters of fluid removed, and sixteen times ten years before and 134 liters removed. In the intervals the condition had been fairly good. A striking feature in some of these cases was the good general condition despite ascites at intervals over a long peirod.

Pain. This was a marked feature in 34 cases. In 10 it was described as abdominal, in 12 referred to the epigastrium, and in 7 to the upper right quadrant of the abdomen. In 2 it was described as in the right back, in 2 it was said to be in the liver itself, and in one referred to the region of the navel. Several of the patients complained of the pain being worse on lying down.

Bowels. No special features were shown. A few of the patients complained of diarrhea and a number described clay colored stools.

Examination. The general findings are discussed first and then the special changes in the liver.

General Condition. A striking feature was *emaciation*, which was marked in 29 cases, and in some was extreme. A number of other patients had lost some weight but could not be described as emaciated. The appearance of many of the patients suggested severe illness. Jaundice was present in 23 cases. The degree varied from a slight to a marked jaundice, the color of three being greenish yellow. A striking feature was the rapidity of clearing of the jaundice under treatment.

Fever. There was some elevation of temperature in all but 7 cases of the series. This is a point of some importance in reference to diagnosis, as the persistence of fever had led to tuberculosis being suspected in some cases. The temperature in about two-thirds of the cases showed constant elevation. In the majority this was not very high, the record being 99° and 100° and 101° F. In some cases it was steadily between 100° and 102° F. In the other cases the temperature was not constantly elevated but rose each day. In the majority the highest point was not over 102° F., but in 3 cases it rose to 103° and 104° F. In some cases these elevations were accompanied by chills.

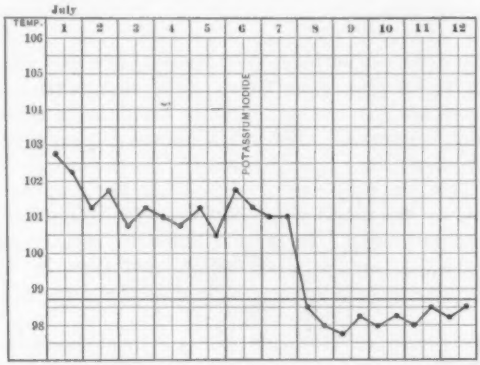

FIG. 1.—Showing the effect of potassium iodide on the fever.

The influence of treatment on the fever was very marked in almost all the cases in which fever was present. In one patient the temperature fell to normal in twenty-four hours and remained there, but the most common period required was forty-eight hours. This was the case in 11 cases. In 5 cases three days were required, and in 5 other cases the temperature reached normal in 6 days or less. This result followed the administration of potassium iodide in the majority of cases; in some mercury was given also, but the most striking results were obtained with potassium iodide alone (Fig. 1).

Blood. The average count in 30 cases was: Hemoglobin, 71 per cent.; red cells, 4,380,000 per c.mm., and leukocytes, 8400 per c.mm. In 12 cases the leukocytes were over 10,000 per c.mm., the highest count being 13,000 per c.mm. In only 2 cases was the red count below 3,000,000, the lowest being 2,700,000 per c.mm. In 4 cases the count was between 3,000,000 and 4,000,000. The differential count showed some variation in certain cases, but there were no striking constant peculiarities.

Ascites. In 23 cases this was present and usually the fluid was large in amount. Tapping was done in 11 cases. This may seem a small proportion, but one of the striking features is the rapid disappearance of the ascitic fluid under proper treatment without tapping being required. Of the 11 patients one tapping was sufficient in 4, 4 were tapped twice, 1 required to be tapped three times, and 1 was tapped thirteen times. The amount removed at one tapping varied from 2.5 to 22 liters. This last figure seems very large; the patient was admitted twice within six months and was tapped once on each admission, the amounts removed being 19 and 22 liters. She presented a remarkable appearance before each tapping and after it the improvement was striking. She was a colored woman, who refused to remain in the hospital long enough to receive thorough treatment. The specific gravity of the ascitic fluid varied from 1008 to 1020 and the albumin content from 8 to 40 grams per liter. The predominant cells were small lymphocytes. In the only case in which the ascitic fluid was tested for the Wassermann reaction this was not given. Instances of a positive result have been reported.

Spleen. This was palpable in 24 cases, in the majority of which the enlargement was marked, in some the edge being several inches below the costal margin. In 8 other cases the area of dulness was increased. The spleen was always hard and firm; in no instance was any irregularity felt; in one case a splenic gumma was found at autopsy.

Liver. The changes in this organ are most important in the discussion of the subject. It is convenient to divide the cases into the congenital and acquired.

1. *Late Congenital Syphilis.* Of the late congenital cases there are three instances, which show considerable similarity in the findings. As Rolleston insists we must be very careful not to mistake acquired cases for congenital ones. If acquired it must be at an early age and usually from accidental infection. In these three cases the age of onset of symptoms was two, twelve, and sixteen years. In the first case the mother had two miscarriages, but the child showed no sign of syphilis other than the hepatic condition. In the second there was chronic ear disease dating from the age of four and rhagades at the corners of the mouth. Three other children of the family died soon after birth. In the third case there were no other signs of syphilis, but the father had a syphilitic infection for which he had taken very little treatment.

In these cases the liver showed much the same condition. It was much enlarged generally and showed remarkable, large, rounded, smooth swellings in the epigastrium, which caused distinct prominences (Fig. 2). In one of the patients exploration was done and the mass was found to be a prominence on the surface of the liver which did not differ in appearance from the rest of the organ. It

was distinctly softer than the liver tissue elsewhere and there were many adhesions between it and the abdominal wall. A portion removed for examination showed some increase in connective tissue, but not much more. A positive Wassermann reaction was given by this patient and marked improvement for a time followed the giving of mercury and potassium iodide. He died about four years later, and apparently from the resulting cirrhosis. In 2 of these patients there was in addition a small nodular mass felt on the right lobe. The spleen was much enlarged in 2 and the area of dulness increased in the other. All 3 patients had fever. Ascites was present in 2 of them.

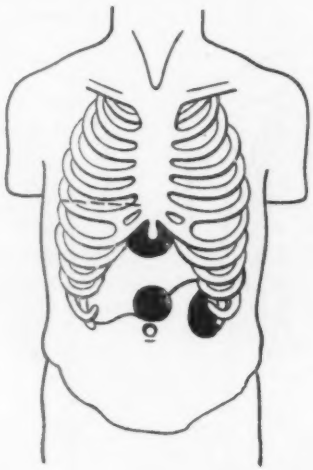

FIG. 2.—Large rounded prominences in late congenital syphilis. Enlargement of spleen

2. *Acquired Cases.* In the study of the tumor one point is worthy of special emphasis, and that is the relatively marked involvement of the left lobe as compared with the right in many of the cases. In 53 cases (3 others being regarded as congenital) the liver was enlarged or showed a tumor mass in 49, and in 23 of these the involvement of the left lobe was strikingly marked in comparison with the right. This is an important point in diagnosis. In regard to the changes in the liver the cases may be divided into three groups.

(*a*) With general enlargement but no marked gross irregularity of the surface (20 cases). In some cases the liver was slightly irregular.

(*b*) With definite nodules (20 cases).

(*c*) Showing a marked prominence which might be described as a boss sometimes associated with nodules elsewhere, but the large smooth enlargement being the striking feature (9 cases). In 3 cases regarded as late congenital this condition was present.

(*a*) *General Enlargement.* The extent of this varied from an edge which was two inches below the costal margin to cases in which the edge was below the navel. The surface was smooth and the liver hard in the majority; in 2 cases the surface was slightly irregular (Fig. 3). In 8 cases there was complaint of pain and tenderness on palpation. The spleen was enlarged in 12 cases and in 8 ascites was present. There was marked distention of the surface veins in 7 cases. Fever occurred in 14 cases. It is easy to

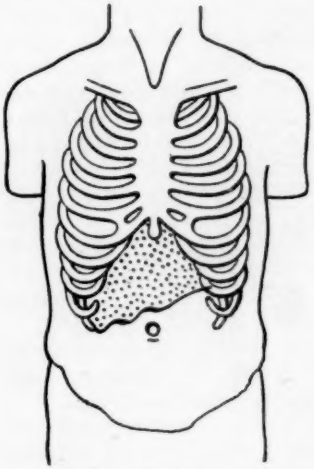

FIG. 3.—General enlargement of the liver, the surface having a slightly irregular character.

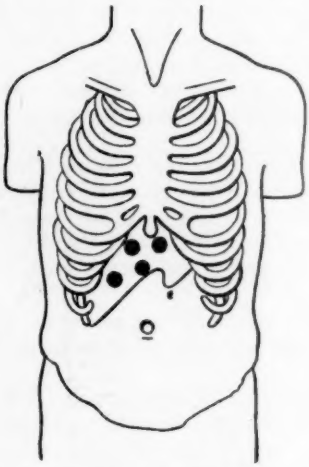

FIG. 4.—Nodules on the surface of the liver.

see that ordinary cirrhosis would be suggested in the cases of this group. Actually, this mistake did not occur in the cases of this group. The incorrect diagnoses were: One was thought for a time to be hepatic abscess on account of fever, chills, and sweats, but the condition was recognized later; 2 had cerebral lues which dominated the picture; 2 had severe cardiac disease, to which the enlargement of the liver was ascribed.

(*b*) *Nodules.* In the majority these were particularly evident in the epigastrium or in the adjoining part of the right hypochondrium (13 cases) (Fig. 4). In 3 they were more or less general over the surface of the liver and in 3 there was a very large irregular nodular mass. Ascites was present in 10 cases. The spleen was

enlarged in 14 cases. Prominence of the surface veins was marked in 8 cases. Fever occurred in 17 cases. The relatively marked involvement of the left lobe was marked in many of the cases of this group. The error in diagnosis most to be expected would be neoplasm. This occurred in one case, exploration being done, which gave the diagnosis. In one case there was colloid carcinoma of the peritoneum; one was diagnosed as hypertrophic cirrhosis until on a subsequent admission he returned with a tubercular syphilide eruption; one had tuberculosis and the liver condition was regarded as amyloid (which was the case); and in one there was acute leukemia, the diagnosis of syphilis not being made until autopsy. Tuberculous peritonitis was the diagnosis in one case with ascites, the nodules in the epigastrium being regarded as a nodular thickened omentum.

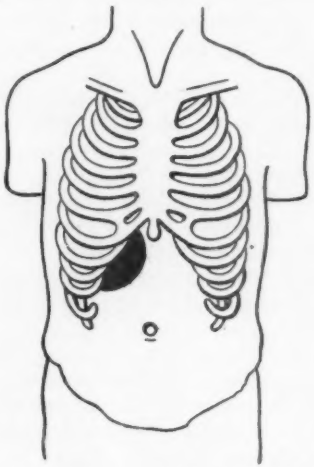

FIG. 5.—Large rounded mass projecting below the right costal margin.

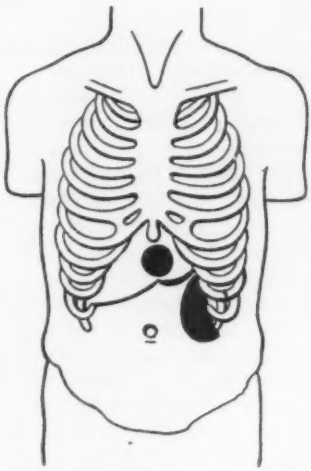

FIG. 6.—Large tumor with a rounded prominence. Marked enlargement of the spleen.

(*c*) *Rounded Tumor.* The size was enormous in some cases (Figs. 5 and 6), there being a large rounded projection which in some filled the whole upper abdomen. In several instances the enlargement of the spleen was remarkable; in 2 cases the organs practically touched and filled the whole of the upper abdomen. Ascites was present in 4 and the spleen was enlarged in 4 cases. In 1 a friction rub was heard over the mass. Fever was present in 7 cases. Only one error in diagnosis was made, the enlargement being regarded as due to malignant disease. Survival for two years and the appearance of a luetic skin eruption (rupia) gave the correct diagnosis.

Diagnosis. This may give difficulty in three principal ways. In the first there is another condition, such as cardiac disease, which seems sufficient to account for the symptoms; this is especially likely to occur if the liver is not specially enlarged or if with enlargement the surface is smooth. In other cases ascites may prevent the recognition of hepatic enlargement. In the second group, disease of the liver is recognized, but its nature is not realized. In the third group some other abdominal condition, such as tuberculous peritonitis, is thought to be present.

1. In 8 cases some other condition was diagnosed. In 3 cases there was cerebral syphilis, the symptoms of which were prominent. In 2 cases tuberculosis, and in the same number cardiac disease was present; in one acute leukemia. In all these the diagnosis was correct so far as it went. In one case the patient had tuberculosis, had been a heavy drinker, and alcoholic cirrhosis was suspected. In 2 cases there was advanced cardiac disease, and in the remaining one leukemia was thought to be the cause of the hepatic enlargement.

2. There were 6 cases in this group. In 2 carcinoma and in 2 alcoholic cirrhosis were diagnosed, and in one each, abscess and gallstones.

3. There were 4 cases, in 3 of which ascites was recognized, but its cause was not determined. In 1 carcinoma of the peritoneum and in 1 tuberculous peritonitis was suspected. One of the other cases was in some ways the most remarkable of the series. The patient was a colored man, aged forty-seven years, who complained of swelling of the abdomen and legs, which began one month before. There had been severe abdominal pain. There were ascites and edema of the legs, but the liver and spleen could not be felt. He died in three days after admission. At autopsy the liver was very irregular and showed a large mass of connective tissue which involved the hepatic vein and inferior vena cava. Many gummata were scattered through the liver.

It may be said that in several cases of 2 and 3, the correct diagnosis was made on subsequent examinations; in all of 3 it was made at autposy.

General Symptoms. As is evident from the study of the symptoms there may be a marked change in the general condition. The patient may have lost weight and strength, be somewhat anemic, have had hematemesis and suffered from abdominal pain. Naturally the possibility of malignant disease comes particularly to mind. The occurrence of fever may suggest some infection. In the cases without any enlargement or evident change in the liver (only 4 in this series) only the knowledge of the possibility of syphilis of the liver, the search for proof of infection (especially the Wassermann test) and the results of specific treatment could give the diagnosis. In this connection the necessity of keeping syphilis in mind as the

cause of more or less continued fever should be emphasized. It is very evident that with advanced cardiac or renal disease, tuberculosis, etc., in the absence of any special hepatic features the diagnosis is not likely to be made.

Recognition of the Liver Condition. Here there are several conditions which have to be considered, especially the diagnosis (*a*) from ordinary hepatic cirrhosis, which is most likely to occur in the cases of uniform enlargement; (*b*) from newgrowth, either of the liver, or in some cases, in which there is a single nodule, from newgrowth of the stomach. This is most likely in cases with marked nodular changes in the liver. (*c*) In the cases with the large, smooth, dome-like tumor, abscess or cyst may be considered. (*d*) Ascites may give difficulty, and it is very important to palpate the abdomen immediately after tapping. It may only be possible then to feel an enlarged liver or a small nodule. Of less importance are (*e*) amyloid disease, (*f*) cholelithiasis, (*g*) splenic anemia, and (*h*) Hodgkin's disease.

There are some points which deserve emphasis in this connection. One is a history of previous tapping followed by improvement for a time. There were 7 such cases in this series. Another is the finding of relatively marked involvement of the left lobe as compared with the right. This, with any striking irregularity in the organ, should always suggest the possibility of syphilis. The features of the tumor are especially discussed.

(*a*) *Group with General Enlargement.* This is difficult to distinguish from ordinary cirrhosis, especially as many of the patients give an alcoholic history. Careful examination should be made for any nodular enlargement, and this is particularly important immediately after tapping if there is ascites. In several cases a small nodular mass was felt coming from below the costal margin on deep inspiration, sometimes high up in the costal angle. The liver itself often feels very hard and the surface may be uneven and somewhat rough. Tenderness is sometimes quite marked. It is evident that the distinction from an ordinary cirrhosis is not easy. The knowledge of the possibility of syphilis is perhaps the greatest aid, as it suggests the Wassermann reaction and the therapeutic test. The value of this last is great and of course there need never be any hesitation in doing it, as no harm will result if the condition is not syphilitic. The following is an example of this group:

The patient was a woman, aged thirty-five years, who complained of fever. She had had pelvic infection with a double salpingitis, for which both tubes had been removed some time before. She gave a history of one miscarriage. There had been fever for some months which varied from 99° to 101° F. She had lost considerable weight and at one time the diagnosis of tuberculosis had been made and then again of pelvic infection. At one time on account

of the fever it had been thought that she might have typhoid fever, and the Widal reaction had been done on two occasions, both negative. On examination the patient was emaciated and looked badly. There was no jaundice. The liver was found to be distinctly enlarged and the edge could be felt two inches below the costal margin in the right nipple line. Dulness above in the right nipple line began at the fourth rib. The liver was tender; no nodules were felt. The spleen was markedly enlarged; the edge was felt below the costal margin and was quite hard. There was no rash or evidence of any bone lesions. Diagnoses of typhoid fever, malarial fever, tuberculosis, and septic infection had all been considered. In view of the continued fever and enlargement of the liver it seemed important to consider syphilis. The Wassermann reaction was found to be positive. The patient was put on inunctions and given potassium iodide, and on the third day the temperature dropped to normal and remained there. Within two weeks she had gained 8 pounds and the liver was definitely smaller in size and the edge could just be felt below the costal margin on deep inspiration. The spleen was reduced in size and the edge could just be felt on full inspiration. The patient was seen nine months later; she had gained 25 pounds in weight and looked the picture of health. Neither the liver nor the spleen could be felt.

(*b*) *The Group with Nodular Masses.* The diagnosis here may be very difficult and a nodule in the liver, particularly in the left lobe, may suggest malignant disease in the stomach or bowel or in the liver itself. As an example of the former the following is quoted:

The patient was a white male, aged thirty-one years. He came complaining of digestive trouble. He had a primary lesion eight years before, but had taken very thorough treatment for five years. His present illness dated back one year. He began to feel badly, complained of pain in the epigastrium and a certain amount of nausea, but no vomiting. He had not been jaundiced. He had lost 25 pounds in weight and on examination was emaciated. There was slight fulness in the left epigastrium and on palpation a small nodular mass could be felt which was quite tender. The edge of the liver was just felt in the right nipple line but could not be positively felt in the median line. The spleen was not felt. After inflation of the stomach the nodule was more easily felt, but its situation was not changed. The note over it was tympanitic. Test meals showed a low total acidity with a mere trace of free hydrochloric acid. The blood count showed a secondary anemia.

The diagnosis was between newgrowth of the stomach and syphilitic nodule of the liver. It was very difficult to tell whether the mass was in the stomach or liver. It was decided to watch the effect of specific treatment, and the patient was given inunctions of mercurial ointment and potassium iodide by mouth. The improvement was very striking; the nodule rapidly disappeared in

size and could not be felt within a month. The patient gained weight rapidly and was soon in perfect health.

The masses on the liver may be regarded as evidence of malignant disease, a mistake which it is easy to make if the general features are marked. The following is such a case:

The patient was a white male, aged fifty-four years, who complained of swelling in the abdomen. His present illness had lasted for about a year and began with nausea and discomfort after eating. Jaundice appeared a few months later. He had lost a great deal of weight and there had been marked abdominal swelling. The patient was emaciated and anemic. The abdomen was much distended with a distinct prominence in the upper part on the surface of which irregularities could be seen. On palpation a hard, irregular, nodular mass was felt, with the lower edge considerably below the navel. A little to the left of the navel a definite notch was felt. The diagnosis of carcinoma was made. The patient did not live in Baltimore, and after discharge he was lost sight of for two years, when it was learned from his physician that the patient was still living and had a well marked skin eruption, regarded as syphilitic.

In one case of this kind an exploration was done to determine the cause of abdominal symptoms, the patient having severe pain. Two gummata were found in the liver.

(*c*) A variety of other diagnoses may be made. Abscess of the liver may be suspected, particularly in the cases with chills, sweats, and irregular fever. Such a case is the following:

The patient was a white male, aged thirty-eight years, who came with a history of abdominal pain, great weakness, loss of 20 pounds in weight, and fever with sweating for the last six weeks. He had had a good deal of diarrhea. The patient looked very badly, was anemic, and very sallow. He had several attacks of severe pain in the region of the liver, which was somewhat enlarged and quite tender. There was marked tenderness in the seventh interspace, a little outside the right nipple line. The temperature was very irregular, varying from 98° to 102.5° F., and the patient had a number of profuse sweats. Liver abscess was suspected and a number of exploratory punctures were made over the right lobe of the liver, but nothing but blood was obtained. After this the patient was put on potassium iodide with which the improvement was rapid, the pain disappeared and he gained weight and was discharged well.

The *mistakes* in diagnosis which were actually made as regards the tumor are of interest. In other cases, as when cerebral syphilis was present, the diagnosis was correct, but the liver condition was not regarded as important or there was no enlargement of the liver. In 10 cases a wrong diagnosis of the liver enlargement was made. In 2 of these this was carcinoma; in 1 the diagnosis was

corrected by the duration, the appearance of a specific skin eruption, and the result of treatment; in the other case the patient had both carcinoma of the peritoneum and syphilis of the liver, as was found at autopsy. In 2 cases a diagnosis of hypertrophic cirrhosis was made; in 1 the patient returned a year and a half later with a tubercular syphilide, following which the result of treatment was marked. In the second case syphilis of the liver was suspected, but excluded as the Wassermann reaction was negative. Some months later, however, the Wassermann reaction was positive and the diagnosis was also supported by the result of treatment. One case was diagnosed as cholelithiasis and the proper diagnosis reached through the result of treatment over a year later. In 1 case operation was done to determine the cause of persistent pain and enlargement in the upper abdomen, no positive diagnosis having been made. In one case abscess of the liver was suspected, but the result of specific treatment gave the correct diagnosis. Tuberculous peritonitis was the diagnosis in one, the nodules in the left lobe being regarded as the thickened omentum. Enlargement of the liver from cardiac disease was regarded as the cause in one case; this was present and hepatic syphilis as well. In the last of this group practically every possible diagnosis was made by different men. This was regarded as an instance of late congenital involvement, and in many particulars was like a remarkable case reported by Cheney.[4] Hanot's cirrhosis, angioma, adenoma, Hodgkin's disease, and cyst were all considered in addition to cirrhosis. Even after the abdomen was opened it was not possible to be sure of the diagnosis. A positive Wassermann reaction and the response to specific treatment gave the correct diagnosis.

Therapeutic Test. There must always be some risk of error in trusting to the result of therapy to make a diagnosis, but in this condition the results are so striking that it has to be included as a method of diagnosis. We have both the general effect, shown particularly on the fever, and the local changes in the liver. As already noted, the effect on the fever is usually very striking, in many cases the temperature falling to normal within forty-eight hours. The influence on the liver itself is almost equally marked; two or three weeks may show a marked decrease in the size of the liver as a whole or of prominences on its surface. In some cases the spleen also shows a remarkably rapid decrease in size. While sometimes the enlarged liver in cirrhosis may show a rapid decrease in size, yet this is not likely to cause confusion.

A knowledge of the condition must be regarded as the most important aid to diagnosis. Other signs of syphilis may suggest the diagnosis. The presence of unexplained fever with hepatic symptoms should suggest syphilis and doing the Wassermann reaction. If in doubt the therapeutic test should always be tried.

[4] Jour. Amer. Med. Assoc., March 26, 1910, liv, 1053 to 1056.

Course. Judging from autopsy experience, recovery must be comparatively common. So far as we can decide the hepatic functions are completely restored, as in many patients dying of other diseases and having extensive changes in the liver from syphilis there is no evidence of any disturbance. It is just as certain that a certain number die of the disease and the majority unrecognized. In cases with extensive cirrhotic changes the outlook is practically the same as in ordinary cirrhosis. In such cases we must not expect to do much by treatment.

There were 14 deaths among this series of 56 cases. Of these in only 1 could death be attributed directly to hepatic syphilis. In this case the process caused obliteration of the hepatic veins and inferior vena cava with resulting thrombosis. In 5 cases death resulted indirectly, in 4 from the resulting cirrhosis, and in 1 from amyloid disease. Some of the patients with cirrhosis had received active treatment with resulting temporary improvement. In 1 case death resulted from carcinoma of the peritoneum, in 3 from chronic nephritis and uremia, in 1 from pulmonary tuberculosis, in 2 cerebral syphilis, and in 1 from acute leukemia. In the other cases improvement was the rule as regards the liver condition. Several of these had other serious diseases, such as renal, cardiac, or pulmonary, which affected the general health.

Treatment. This is the usual therapy for syphilis with special emphasis placed on the administration of iodide of potassium. In many of the cases this alone was given with a perfect result. No difference could be observed when mercury was added, but it seems wise to give both drugs. Dramatic results, such as almost immediate disappearance of the fever, reduction in the size of the liver nodules, and rapid gain in the general state and weight were seen when iodide alone was given. One patient gained 25 pounds in a month. Salvarsan was given to 3 patients in doses of 0.5 or 0.6 gram, and in 2 of these mercury and iodide were not given in order that the effect could be watched. Improvement followed in both cases, but not as rapidly as was the case with iodide alone or mercury and iodide. In the third case all three were given.

We must recognize that in some cases while we can influence the syphilitic process in the liver we cannot prevent or materially affect the resulting cirrhosis unless the cases are seen early and recognized.

CONCLUSIONS. 1. Syphilis of the liver presents a very varied clinical picture with prominent general symptoms in many cases, of which loss in weight is marked. The duration of the symptoms may be prolonged and there may be periods of improvement. Fever is a common occurrence.

2. There are features suggestive of hepatic disease in the majority of the cases. Enlargement or tumor is the most common. This may suggest other conditions, epsecially malignant disease.

General enlargement and the occurrence of nodules or large rounded masses are the most common. A striking feature is the relatively marked enlargement of the left lobe as compared with the right.

3. The diagnosis may be obscured by other diseased conditions or the liver condition may be interpreted wrongly. Ascites is sometimes a difficulty. Knowledge of the features of hepatic syphilis and the therapeutic test are important aids.

4. Treatment can influence the syphilitic process, but not its results (cirrhosis, amyloid).

MALTOSE IN INFANT FEEDING.[1]

By John Lovett Morse, A.M., M.D.,

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Three different sugars are used commonly in the feeding of infants, lactose, saccharose, and maltose. Maltose is seldom, if ever, used in the pure form. Almost all of the sugars which are spoken of as malt sugars are in reality combinations of maltose and dextrin, for example: Soxhlet's Nährzucker equals maltose 52.44 per cent., dextrin 41.26 per cent.; Löflund's Nährzucker equals maltose 40 per cent., dextrin 60 per cent.; Mead's Dextri-Maltose equals maltose 51 per cent., dextrin 47 per cent.; Maltose of Walker-Gordon Laboratory, equals maltose 57.1 per cent., dextrin 30.9 per cent.; Mellin's Food equals maltose 60.8 per cent., dextrin 19.2 per cent.

These sugars are all disaccharides, lactose being a combination of dextrose and galactose, saccharose of dextrose and levulose, and maltose of dextrose and dextrose. The dextrins are bodies which are formed in the change from starch to maltose. There are a great variety of them and their exact composition is not well known. The dextrins being finally converted to maltose, their ultimate end is dextrose.

The disaccharides are not absorbed as such from the intestine under normal conditions, but are first broken down into their respective monosaccharides by special ferments. These ferments are maltase, saccharase (invertin), and lactase. They are formed in the mucous membrane of the small intestine. Lactase is more abundant in the upper than in the lower portion of the small intestine. Maltase is also present in the blood, the saliva, and the pancreatic juice. Saccharase is present in the intestinal mucous

[1] Read before the American Pediatric Society, May 30, 1912.

membrane at the beginning of the fourth month of fetal life and maltase at the end of the fourth month. Lactase appears in the seventh or eighth month. Lactase is usually the least abundant at birth, but soon increases when milk is given.

The monosaccharides which are formed are taken up by the portal capillaries and carried by the portal vein to the liver where they are converted into and stored as glycogen, to be later reconverted by the maltase in the blood into dextrose and used as required.

If an excessive amount of a disaccharide is introduced into the intestine, or there is a lesion of the intestinal wall, it will pass into the circulation before it is broken down into the monosaccharides. When the disaccharides reach the circulation in this way or are introduced directly into the circulation, all the lactose and the major part of the saccharose are eliminated unchanged in the urine, there being no ferment in the blood which is capable of breaking down these sugars. The rest of the saccharose is eliminated through the gastric mucosa, the salivary glands, and in the bile. The maltose is, on the other hand, broken down by the maltase in the blood, and unless in great excess, is retained. The limits of assimilation of the disaccharides in infancy are: Lactose, 3.1 to 3.6 grams per kilogram; saccharose, no data, probably about the same as lactose; maltose, 7.7 grams per kilogram.

Maltose is the most quickly absorbed of the three disaccharides, saccharose next, and lactose much less rapidly. On the other hand, however, when equal amounts of these sugars are given, considerably more malt sugar is excreted in the feces than milk sugar (Hartje). In fact, under normal conditions lactose is never found in the feces (Péhu and Porcher) unless the food contains more than 7 per cent. of milk sugar (Hartje).

When the disaccharides are added to a food which contains little or no sugar there is a rapid increase in weight, owing to the lessened elimination of water by the kidneys as the result of the presence in the organism of the products of the assimilation of the sugar absorbed. The gain in weight is more rapid with maltose and saccharose than with lactose, probably because of the more rapid absorption of these sugars.

Finkelstein believes that sugar may cause fever, and in his papers has devoted much attention to the so-called "sugar fevers." Leopold found that 43 per cent. of the babies tested with lactose, 42 per cent. of those with saccharose, and 33 per cent. of those with maltose reacted with fever. This fever was, however, always accompanied by diarrhea, and in none of the cases tested in which the stools remained normal did the sugar cause fever. Schlutz's recent experiments make it appear very improbable, moreover, that, even when there are lesions of the intestine, the rise in temperature is caused directly by the sugar.

The disaccharides are all fermentable. Lactose undergoes lactic acid fermentation more readily than the other sugars. Saccharose undergoes alcoholic fermentation most easily and butyric acid fermentation next most readily, while maltose is especially prone to butyric fermentation and next to alcoholic.

It is generally accepted that under normal conditions, and when not given in excess, lactose and maltose have a slightly laxative and saccharose a slightly constipating action. Leopold has recently found that when lactose, saccharose, maltose, and dextrin-maltose mixtures are given to normal or almost normal infants by mouth in equal amounts, the dextrin-maltose mixtures produce diarrhea less easily than the pure disaccharides and that lactose causes diarrhea more easily than either of the other sugars. Sixty-six per cent. of the babies which were given lactose, 21 per cent. of those given saccharose, 16 per cent. of those which received maltose, and only 5 per cent. of those which took the dextrin-maltose mixtures developed diarrhea. The probable explanation of the greater frequency with which lactose caused diarrhea is its relatively slow absorbability.

It has been claimed that the lactose of cows' milk is not identical with that of human milk. There is, however, no convincing evidence in favor of this claim. No differences having thus far been found in the chemical composition of lactose from different sources, it seems more reasonable, therefore, to consider them identical until they are proved not to be.

The normal fecal flora of the breast-fed infant, according to Kendall, is comprised of the following organisms: Bacillus bifidus, Micrococcus ovalis, Bacillus coli, Bacterium aërogenes, and Bacillus acidophilus. Bacterium aërogenes appears in the upper levels of the tract, the duodenum and jejunum; Micrococcus ovalis in the lower jejunum, the ileum, and to the ileocecal valve; Bacillus coli and Bacillus acidophilus in the region of the ileocecal valve, while the Bacillus bifidus appears to dominate the ascending and transverse colon. The composition and maintenance of the normal fecal flora is without question due to the relative excess of carbohydrate, in the form of lactose, in the milk. Microscopically with the Gram stain, when babies are fed on cows' milk, there is a relative increase in Gram-negative bacilli of the colon-aërogenes type and of coccal forms of the Micrococcus ovalis type, associated with the diminution of the bifidus type. Three butyric acid-forming organisms have been isolated by Passini from the stools of apparently normal bottle-fed babies. These are all anaërobes, and one of them, Bacillus perfringens (Bacterium Welchii) is a cause of a not uncommon type of infantile diarrhea. This organism has also been found by Sittler and many other observers.

It is, therefore, of great importance, in order to maintain the normal fecal flora, to have a considerable amount of sugar in the

food of babies fed on mixtures of cows' milk. According to Kendall, lactose favors especially the development of Bacillus bifidus, which is normally the predominant organism in the large intestine, while maltose is especially conducive to the growth of the Bacillus acidophilus, which, although normally present in small numbers, if present in large numbers is liable to produce an excessive degree of acidity which may cause irritation of the intestine and an intolerance for sugar. Under normal conditions, therefore, as far as regards the maintenance of the normal intestinal flora, lactose is preferable to maltose.

Although maltase is formed before lactase, lactase is present at birth and becomes abundant as soon as milk is given and there is any need of it. The early appearance of maltase is, therefore, no argument in favor of the use of maltose instead of lactose. The presence of maltase in the blood is no argument in favor of maltose as a food. The maltase is in the blood to break down the maltose formed from glycogen, not to break down sugars in the intestine. It is impossible, moreover, for it to get into the intestine. The assimilation limit of lactose is, it is true, lower than that of maltose. This limit is, however, at least three times as large as would ever be given in a properly modified milk. The higher assimilation limit of maltose is therefore of no practical advantage. In spite of its higher assimilation limit, moreover, more maltose than lactose is excreted in the feces when equal amounts are given by mouth. The more rapid immediate gain in weight when maltose is added to a food poor in sugar than when lactose is added is of no importance, since the gain in both instances is almost entirely due to the retention of water. Even if it is true that the so-called "sugar fever" is really due to sugar, the fact that the rise of temperature occurs more often with lactose than with maltose does not count in favor of the use of maltose rather than lactose in the feeding of normal infants, because fever never occurs unless there is a diarrhea which shows some lesion of the intestine. Neither is the fact that large amounts of lactose cause diarrhea more easily than maltose and the dextrin-maltose preparations of much importance, because such large amounts of lactose should never be given. The less rapid breaking down and the consequently slower absorption of lactose than of maltose is of great importance in maintaining the normal fermentative flora throughout the intestinal tract. Few organisms other than those normal to the intestinal tract of infants can utilize lactose before it is broken down, many can utilize maltose. Lactose is especially suited to the growth of the Bacillus bifidus, the organism normally predominant in the large intestine; maltose to the development of the Bacillus acidophilus, which, when in excess, may cause disturbance. It is not necessary, therefore, to bring forward the argument that lactose is the only sugar present in human milk and in the milk of other animals and that it must be

therefore the natural sugar for an infant, because, in the light of the evidence just cited, there can be no doubt that lactose is preferable to maltose for the feeding of normal infants.

Finkelstein and Meyer believe that the diarrheal diseases of infancy originate in a functional weakness of the intestine, that this functional weakness is kept up and increased by fermentation, and that sugar is the special and primary cause of fermentation. Neither normal or abnormal acidification can take place without it. The fat is never involved primarily. It is injurious in that it causes an acid fermentation. The fermentation of the sugar is dependent on two main factors: The concentration of the whey, and the relative proportions of casein and sugar in the mixture. They conclude, therefore, that the principles on which the preparation of a food to combat intestinal fermentation depend are: A diminution in the quantity of milk sugar; a diminution of the salts through dilution of the whey; and an increase in the casein, with varying, and, under certain circumstances, not inconsiderable amounts of fat. They consequently developed a food to meet these indications, to which they gave the name "Eiweissmilch." This food is prepared with precipitated casein and buttermilk, after which it is boiled. Its composition is: Fat, 2.5 per cent.; lactose, 1.5 per cent.; proteid, 3 per cent.; salts, 0.5 per cent.

They claim that with this mixture the loose, green stools are quickly replaced by typical soap stools. One quart of this milk contains, however, only about 370 calories. Babies taking it suffer, therefore, from lack of nourishment. They advocate, therefore, the addition of malt sugar or the dextrin-maltose preparations to the mixture after the disappearance of the acute symptoms in order to avoid loss of weight and disturbance of nutrition. They claim that, on account of its more rapid absorbability, maltose does not cause a recurrence of the symptoms of fermentation.

Finkelstein and Meyer's arguments point strongly to sugar as the etiologic factor in intestinal fermentation. Their treatment of fermentative conditions with a food low in sugar and high in proteids is therefore a rational one. The substitution of dextrin-maltose mixtures for lactose also seems rational. It does not seem rational, however, to treat all cases in the same way or to give all babies the same food without regard to their individual digestive capacities. The lactic acid in the buttermilk also seems irrational in that it is one of the products of the fermentation of lactose and, therefore, presumably one of the substances causing the disturbance in the intestine.

It seems wiser to take advantage of the main principles of this method of treatment of the intestinal fermentative conditions and avoid the disadvantages of a routine food and the unnecessary, even if not harmful, lactic acid. It is possible by using mixtures of precipitated casein, prepared according to Finkelstein and

Meyer's method, water and cream to obtain any desired percentages of fat and casein with extremely low percentages of lactose and salts. Any of the dextrin-maltose preparations can then be added in any quantity desired. The use of this method of treatment in a considerable number of cases during the last year has convinced me that there is a variety of intestinal indigestion in infancy which is relieved by reducing the sugar and salts in the food to a minimum and giving large amounts of casein and that the dextrin-maltose preparations can be given to these patients sooner than lactose without causing a return of the symptoms. This type of intestinal indigestion may be either acute or chronic and is characterized by an increased number of stools of diminished consistency, green in color, often frothy, acid in reaction, and not infrequently containing mucus and fat curds. Unfortunately, however, precisely similar stools may be seen in other conditions in which the trouble is due primarily to bacteria and in which this method of treatment may do material harm. It is to be hoped that with increasing knowledge of the bacteriology of the intestinal tract in infancy some simple methods will be evolved which will make it possible to readily differentiate between the diarrheas due primarily to chemical changes in the intestinal contents and the disturbances of the digestive functions dependent on them and those due primarily to bacteria. At present it is extremely difficult to distinguish between them and correspondingly hard to know how to treat them.

There is a type of diarrhea in infancy, usually characterized by watery, green, foamy, irritating stools, but sometimes with discharges of mucus and blood, which is associated with the presence in the intestinal contents of large numbers of bacilli belonging in the group of which the Bacillus perfringens and the gas bacillus (Bacterium Welchii) are members. These organisms ferment the common disaccharides and liberate considerable amounts of butyric acid. Large amounts of sugar are, therefore, contraindicated in this group of cases, maltose being more harmful than lactose because it undergoes butyric acid fermentation more readily. This type of diarrhea yields most rapidly to buttermilk and mixtures containing living lactic acid bacteria with a small amount of lactose. The lactic acid forming organisms kill out the pathogenic organisms. Being themselves fermentative organisms, they cannot develop in a protein medium. A moderate amount of lactose must, therefore, be present in the food.

It has been shown by Theobald Smith, Kendall, and others that when bacteria act upon carbohydrate and proteid substances they produce from the former fermentative products and from the latter putrefactive substances. The fermentative process takes precedence over the putrefactive if both carbohydrate and proteid are present together in the medium in which they are. The products

of the fermentation of carbohydrates are practically harmless, while the products of the decomposition of proteids are actively toxic. In the diarrheal diseases due to organisms, such as the dysentery bacillus, which produce toxic substances from protein, it is therefore of great importance to have an excess of readily fermentable carbohydrate in the food to change the character of the bacterial activity from the proteolytic to the fermentative type. This is most easily accomplished by the feeding of the disaccharides, which are preferable to the monosaccharides, because they are more readily procured and especially because they are less rapidly absorbed from the intestinal tract, and to the polysaccharide, starch, which, if given in sufficient amount to accomplish the desired result, is almost certain to disturb the digestion. Starch is broken down so slowly, moreover, that there is never a sufficiently great concentration of sugar at any time. Lactose is preferable to maltose for several reasons. It is, in the first place, more slowly broken down and absorbed and consequently exerts a more prolonged action. In the next place, few organisms, except those normal to the intestinal tract of infants, can utilize it before it is broken down by hydrolysis. There is also danger, as already pointed out, if maltose is given freely, of encouraging the overdevelopment of the Bacillus acidophilus and developing a sugar intolerance.

CONCLUSIONS. Lactose is for many reasons preferable to maltose for the feeding of normal infants. There is a type of intestinal indigestion due to the fermentation of sugar in the treatment of the convalescent stage of which maltose is better borne than lactose. Maltose is contraindicated in the treatment of diarrheas due to the gas bacillus and similar organisms, and is less useful than lactose in the treatment of those caused by the dysentery bacillus.

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BISMUTH POISONING.

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It seems rather strange that there should be no adequate discussion or description of the lesions caused by intoxication with bismuth in any modern text-book on medicine. Even in Edsall's exhaustive article on metallic poisons in Osler's *System of Medicine* there is no mention of the effects of bismuth upon the human system. This is all the more remarkable in view of the fact that evidences of systemic poisoning by bismuth are scattered through the literature of the last few years, especially since the advent of the *x*-rays in the diagnosis of gastro-intestinal diseases and of bismuth paste (Beck's) in the treatment of chronic suppurating, non-bacterial sinuses.

A case of bismuth poisoning following the injection of about 2 ounces of bismuth subnitrate paste into an iliopsoas abscess, revealed the utter absence of data on the subject in an available form, and constitutes the excuse for the present *resume* of the subject.

Experimental Data. As long ago as 1786 there were reports of vomiting, diarrhea, twitchings, dizziness, and somnolence due to the ingestion of bismuth salts. It was thought that these symptoms were due to impurities, particularly arsenic and lead, in the preparations of bismuth used, and it is possible that such was the case at that time.

Even before Kocher, in 1881, recommended bismuth subnitrate salve in the treatment of burns and granulating wounds, there had been some experimental evidence that bismuth salts were not altogether harmless.

Feder-Meyer,[1] in 1879, investigated the subject. He says that according to Orfila, all bismuth preparations containing oxygen are toxic, whether taken internally or injected into a vein. Feder-Meyer produced acute and chronic poisoning in rabbits by injecting soluble ammoniated bismuth citrate subcutaneously or by introducing it into the stomach through a tube. In acute poisoning the animals had convulsions and incoördinated movements ending in death. There was fall of blood pressure and of body temperature. In chronic poisoning the animals were restless and lost weight. When the dose was increased, there were twitchings and diarrhea ending in convulsions and death. He found that the subcutaneous injection of from 6 to 9 milligrams of the salt per kilo body weight, caused death of the animal. The heart

[1] Inaug. Dissert, Würzburg, 1879.

muscle and liver showed fatty degeneration. In the mucous membrane of the stomach there was pigmentation due, he thought, to extravasation of red blood cells, and in most of the organs there were demonstrable quantities of bismuth. He thought that death was due to poisoning of the nerve centres.

Mory,[2] in 1883, repeated the experiments of Feder-Meyer using the same bismuth salt, but he regarded the death of his animals as a heart paralysis. In cats and dogs the subcutaneous injection of 0.15 gram ammoniated bismuth citrate caused vomiting and diarrhea. In chronic poisoning he saw increasing destruction of the skeletal muscles and thought that the paralysis was due to this condition. He concluded that the bismuth salts are also intense poisons to the higher animals. In warm-blooded animals we can explain all the symptoms by the action of bismuth upon striped muscle. The longer the poisoning lasts the more intense the gastro-intestinal symptoms become. There is marked hyperemia of the intestines accompanied by a fall in blood pressure. The animal dies because the heart has no resistance against which to work.

Luchsinger[3] experimented upon rabbits, cats, and dogs, and came to the same conclusions as Mory.

In 1886, Dalché[4] reported 2 cases of bismuth poisoning in humans characterized by black line on the gums and white diphtheritic membranes. There was bismuth in the urine. He and Villejean[5] instituted a series of experiments on the toxicity of bismuth subnitrate. Already the nephritis, enteritis, and stomatitis with discoloration of the gums had been attributed by observers to the bismuth salts. Dalché himself, however, in his case reports had suggested that impurities, particularly lead and arsenic, were to be considered as factors. These observers satisfied themselves by careful analysis of the purity of their bismuth salt. They found that they could give to a normal dog 10 grams of the subnitrate daily for a month, in all 300 grams, without noting any ill effects. But when the salt was put on a raw surface of any extent, intoxication often followed. Having shown the toxicity of the salt, they injected dogs subcutaneously with doses of 0.3 gram to 3 grams. For example, one dog on twelve successive days received subcutaneous injections of the salt. It died on the thirteenth day. Five days before death there was noticed on the gums of the anterior molars, on the mucous membrane of the inferior maxilla, at the external alveolar border, a brownish-violet, glistening, serrated line and two brownish-violet spots were seen on the mucous membrane of the left cheek not far from the commissure. The follow-

[2] Inaug. Dissert., Bern, 1883.
[3] Mittheil. d. Naturf. Gesellschaft in Bern, 1882–1883, p. 26.
[4] Annales d'Hygiene Publique et de Méd. Légale, 1886, xvi, 358.
[5] Arch. Gén. de Méd., 1887, xx, 129.

ing day, the eighth, similar spots appeared on the mucosa of the right cheek and the gingival serrated border was advancing. During the succeeding days the serrated border extended upon the anterior gums of the lower jaw and appeared upon the buccal, labial mucosa, and on the inferior surface of the tongue. The oldest lesions became superficially gangrenous and presented softened grayish-white plaques surrounded by a slight areola of a brownish-violet color. At autopsy, besides the lesions described, there were seen enormous superficial gangrenous plaques upon the buccal side of the cheeks. The urine contained no albumin and the kidneys showed nothing but vascular congestion.

A second dog also showed lesions on the gums and on the mucous membrane of the cheeks.

They found that bismuth was eliminated through the salivary glands and that the presence of albuminoid substances favored the solution of the bismuth when in an ordinarily insoluble form such as the subnitrate.

Dalché and Villejean remark that the most striking feature of bismuth poisoning is the stomatitis. It is characterized by a lesion on the gum of a blackish or brownish-violet shiny character, and by spots of similar color on the internal surface of the lips and cheeks. It may remain stationary but in advanced stages the mucosa of the gum margin is softened, the teeth are, at times, loosened and the mucous membrane softens, becomes pulpy and covered with a grayish or whitish-gray membrane surrounded by a blackish areola. These sloughs may separate and ulcers result.

The lesion usually begins at the level of the molars opposite the opening of the parotid gland duct. This is a point common to both bismuth and mercurial stomatitis, as well as the ulcer beneath the tongue where it is in contact with the teeth. In both forms of poisoning salivation is profuse and the breath has a fetid odor.

The stomatitis may follow a few days after the bismuth injection. They conclude that subnitrate of bismuth absorbed from subcutaneous injection or from the surface of a wound, can cause acute intoxication due directly to bismuth. This absorption is due to the presence of albuminous material favoring the solubility of the metallic oxide, although slowly, it produces poisoning because it is continuous. The accidents, stomatitis, nephritis, enteritis, etc., are dependent upon the paths of elimination of the metal.

In a further series of experiments Dalché and Villejean[6] produced chronic poisoning in dogs by injecting 0.25 to 0.50 gram subcutaneously at intervals of a few days for three months. Hemiplegia and stomatitis with a black line on the gums developed and the dog, after becoming weak and emaciated, died. At autopsy the

[6] Bull. de Therapeutique, Paris, 1888, cxv, 404 and 448.

stomach and intestine were full of bile. The large intestine showed pseudomembranous colitis with the usual blackish discoloration; there were congestion and ecchymoses. The liver and kidneys were congested. Careful examination of the peripheral nerves and of the anterior roots revealed nothing abnormal.

They call particular attention to the similarity of stomatitis caused by lead, mercury, and bismuth, lead being less severe because it is not easily absorbed except under certain conditions of peculiar susceptibility. Mercury stands midway between lead and bismuth. The stomatitis may be mild or fatal. All produce dysenteric stools, all act as cholagogues, all produce kidney lesions of greater or lesser severity depending on the dose and on the susceptibility of the animal. They say it is a striking fact that chemically lead, mercury, and bismuth have high atomic weights, 206.4, 200, 210 respectively. They suggest that possibly all the heavy metals copper, platinum, iridium, gold, if absorbed in sufficient quantity would produce similar lesions. Normally bismuth subnitrate is not soluble in the juices of the alimentary canal. Its sojourn in the intestines is short. Two factors concur in rendering bismuth soluble when injected subcutaneously: (1) Profound changes which take place when bismuth oxide comes into contact with tissue juices rich in albumin; (2) the continuous absorption of small amounts now rendered soluble.

Balzer[7] confirmed the work of Dalché and Villejean except that he used citrate of bismuth. He did not think that the stomatitis due to the bismuth is similar to that due to mercury. The bismuth tends more to a membranous formation and appears deposited on the margins of the gums. There is also not so much loosening of the teeth with bismuth and not so much pus due to growth of mouth bacteria. He found that bismuth was eliminated in the urine, bile, and saliva.

Pisenti[8] in an experimental study of the action of bismuth on the organs of the rabbit, found that there were lesions in various organs. In the kidneys there was necrosis of the epithelium of the convoluted tubules. In the digestive system there was partial hyperemia and partial pigmentation without destruction of the mucosa. The liver cells were the seat of fatty degeneration.

Mayser,[9] in a long article, quotes from all the literature up to 1892, and adds some experimental data of his own. He considered that the black pigmentation in the large intestine was due to bismuth sulphide and not to extravasated blood, as Mory and Feder-Meyer had thought. Chemical examination showed bismuth in the blood, urine, stomach, small and large intestine, and kidneys, but not in the bile, brain, or muscles. He concluded from his experi-

[7] Comptes Rendus d. Séances et Mémoires de la Soc. de Biol., Paris, 1889, n. s., 1, 537.
[8] Annali Universita Libera di Perugia, 1887–1888, iii, 87 to 106.
[9] Inaug. Dissert., Freiburg in Baden, 1892.

ments that bismuth has a poisonous effect on the kidneys causing necrosis of the tubular epithelium and a production of casts. The necrosis proceeds slowly and does not lead to great loss of substance. He saw calcified deposits here and there. At times one-half of the kidney contained them, the other half was free. The glomeruli were, at times, calcified. He compared his findings to those produced by chromic acid and mercury nephritis. The calcification found was apparently caused by long-standing, mild poisoning. The most severe changes followed subcutaneous injections, due to the better absorption of bismuth when given in this manner.

Although there are some minor differences in the conclusions of these authors, they are in substantial agreement concerning the toxicity of bismuth when given to animals. In all cases great care was taken to employ only absolutely, chemically pure bismuth salts.

Böhme,[19] in 1907, reported a fatal case of poisoning following the internal administration of bismuth subnitrate, in which the symptoms were violently acute and were like those described by Collishon in nitrite poisoning. There was methemoglobinemia before the child died. This led him to investigate the breaking up of bismuth subnitrate in the intestinal canal. Collishon had already stated his belief in 1889 that the toxic symptoms due to nitrite poisoning and those due to poisoning following the administration of bismuth subnitrate were the same. He, therefore, thought that the nitrites, not bismuth, were responsible for the symptoms.

Böhme showed that bismuth subnitrate in contact with the feces liberated nitrites. He also found that when colon bacilli were grown in bouillon to which bismuth subnitrate was added, that nitrites were formed. Since Böhme's report several fatal cases have been published in all of which there were cyanosis, collapse, diarrhea, and the blood was of a chocolate color before death. The color was due to methemaglobin. In certain cases of intestinal disease the administration of bismuth subnitrate followed by death may be due to the sudden liberation of nitrites, but it cannot be doubted that, in view, of the experimental evidence, bismuth is the toxic agent in the chronic forms surely and in the fatal cases where it has been applied to raw surfaces as bismuth paste.

Case Report. L. N., Hosp. No. 10068, a white girl, aged nine years, of Finnish parents, was admitted to the Milwaukee County Hospital, September 9, 1911, complaining of sore mouth. Her home surroundings have always been of a squalid kind. Both parents probably have syphilis, one certainly had syphilis before this child was born. One sister, aged seven years, died in this hospital of generalized tuberculosis. The patient had never been

[19] Arch. f. exper. Path. u. Pharmakol., Leipzig, 1907, lvii, 441 to 452.

a robust child. In January, 1910, she was in a hospital on account of a weak back. A diagnosis of tuberculosis of the spine was made and she lay on a Bradford frame for one year. During 1910, there was an iliopsoas abscess which pointed at the front of the leg opposite the lesser trochanter. This abscess was twice incised, once above Poupart's ligament, once below. In November, 1910, about 2 ounces of bismuth subnitrate paste (Beck's) were injected into the sinus. The opening of the sinus in the leg below the groin promptly closed and no paste ever was extruded. Within two weeks a black line was noticed at the gum margins. This has persisted, becoming occasionally more prominent, again less noticeable. In August, 1911, a "sore" started in the right cheek opposite the upper second molar tooth. Later there was ulceration of the right side of the tongue.

On admission the child was enveloped in a plaster cast from armpits to the crests of the ilia. On examination, after removal of the cast, she was seen to be well nourished and of normal size. There were evidences of old rickets on the head and chest. The chest was, however, fairly well formed, but flaring below. There was slight impairment of the percussion note beneath the left clavicle with prolongation of expiration. There was a scar about 3 cm. long in the right iliac fossa and a small puckered scar on front of the right thigh. The spleen was palpable. There was general glandular enlargement, especially a large collection of glands beneath the ramus of the right mandible causing a visible swelling. The breath was very fetid, the teeth yellowish, many were decayed, especially those of the lower right jaw. The front teeth were not notched but were roughened both laterally and on the edges.

On the gum margins of both jaws both on the inner and outer sides there was a dark violet-black line averaging 1.5 mm. in depth, which did not quite reach the free border of the gum margin (Figs. 1 and 2). This line was smooth and somewhat glistening. The teeth were not loosened and there was very little pyorrhea alveolaris. The tongue was heavily coated with a brownish fur. Along the whole right edge of the tongue extending nearly to the tip was a bluish- or violet-black discoloration which in its widest part was 2 cm. and extended toward the dorsum and ventral surfaces for a short distance and having rather sharply defined margins. Along the very edge of the tongue in the centre of the discoloration was a white, opaque, serrated membrane, which was adherent to the underlying tissues. On the buccal surface of the right cheek were two discolored plaques, one near the angle of the mouth and one (the earlier one) with its centre about opposite the upper second molar tooth. This latter was 2.5 to 3 cm. in diameter, the former was irregular in outline and smaller. They had exactly the same appearances as the ulcer on the tongue.

The blue discoloration was sharply demarcated from the surrounding fairly healthy mucous membrane. White necrotic serrated membranes covered about half of each ulcer, the centre of the patch corresponding to the centre of the necrotic cap.

FIG. 1.—Showing the line on both gums and the somewhat notched incisors

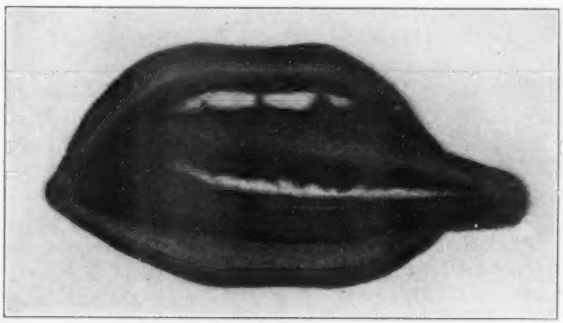

FIG. 2.—Extensive ulceration of the tongue with the diphtheritic membrane.

An *x*-ray of the right lumbar region (Fig. 3) showed an irregular shadow in the lumbar muscles about 10 cm. long and 2 to 4 cm. broad from which delicate shadows ran to the opening of the sinus in the upper leg. This was evidently about 2 ounces of bismuth paste which did not appear much encapsulated.

The Noguchi reaction was negative on two occasions. The red blood corpuscles were, 5,600,000; leukocytes, 14,600; hemoglobin, 90 per cent. (Sahli) on admission. (The leukocytosis was evidently due to the alveolar abscess on the right side.) The differential count of the white cells showed nothing abnormal. The urine was of 1020 to 1025 specific gravity, contained no

albumin nor casts, and on several examinations no bismuth could be found.

The patient gradually improved. The ulcers in the mouth became less foul, the breath became much less fetid. When she left the hospital, February 19, 1912, the following note was made: The condition has practically cleared. The tongue is perfectly clean on the right margin. On the right cheek is a very slight

FIG. 3.—Sketch from x-ray plate showing location of bismuth.

violet discolorated area corresponding to the large spot of ulceration. The breath is no longer disagreeable. The line on the gums, both within and without is still present.

This case is almost the exact counterpart of those reported by Gaucher and Ballé.[11] They record the fact that Kocher in 1881, after his recommendation of bismuth for dressing wounds, reported

[11] Bull et mém de Soc des Hôp de Paris, Paris, 1895, s. 3, xii, 773.

4 cases of poisoning, in 1 of which a blackish discoloration appeared on the gums at the alveolar dental border the day after the dressing to a large raw surface. Petersen in 1883, they remark, also observed a case in a girl, aged fourteen years, following operation and dressing with bismuth subnitrate. There was stomatitis and salivation.

Among other case reports are those of Mahne,[12] E. G. Beck,[13] David and Kauffman,[14] Don,[15] etc.

Symptoms. From the cases reported we can deduce a rather typical picture which differs from the poisoning of lead and of mercury.

There are three stages: (1) Benign, where the violet-black line is the only manifestation; (2) moderately severe, where there is stomatitis, more or less acute, to which succeeds a chronic stomatitis characterized by discoloration of the gum margins and tatooing of the mucosa which extends to the buccal cavity; (3) a severe form characterized by a longer duration of the stomatitis, the margins of the gums and tattoo-like plaques ulcerate, secondary infections supervene, and general symptoms as fever, hiccough, vomiting, diarrhea, and albuminuria occur.

Prodromal symptoms are slight or, if present, there is only malaise, slight salivation or tenderness about the mouth. There soon follows the line on the gums or tattoo plaques and ulcerations on the buccal mucosa. The bismuth line occupies a part or all of one or both jaws. It resembles the lead line but differs from it because of its really violet tint. In benign cases the gum margin is not swollen. In severe cases there may be swelling, ulceration, and loosening of the teeth. Cessation of the bismuth treatment brings about improvement, but the gums still retain the discoloration for some time.

The line on the gums is usually the first symptom of the poisoning, but occasionally there are plaques on the buccal mucosa like tattoo marks. The bismuth plaques may be found anywhere in the mouth but show preference for sites where the teeth and gums come in contact and the first plaque is often at or near the opening of the duct of the parotid gland. The ulceration is more apt to occur at this situation. The sides of the tongue are also frequent sites of ulceration.

The color is the same in all, a violet black. The lesions rarely appear insidiously, but are usually preceded by salivation and erythematous stomatitis. At times the lesions come on rapidly with edema.

The spots may be simply small areas of bluish violet-black color, in severer cases there is some swelling and a diphtheritic

[12] Berl. klin. Woch., 1905, xlii, 232.
[13] New York Med. Jour., 1909, lxxxix, 16.
[14] Illinois Med. Jour., 1909, xvi, 370; Jour. Amer. Med. Assoc., 1909, lii, 1035, 1953.
[15] British Med. Jour., 1909, i, 1481, and 1908, ii, 1604.

white membrane in the centre. This is characteristic of bismuth. In very severe cases gangrene occurs with resulting loss of substance.

The breath is usually foul, depending upon the state of the lesion.

The spots appear simultaneously or in crops. They cause more or less functional disturbance and thus tend to weaken the patient. Mastication may become impossible. The swollen and painful tongue may with difficulty be protruded. Ulcerations on the soft palate and tonsils may cause hoarseness. Salivation is marked and when healing of ulcers begins the saliva may be so tenacious as to interfere with swallowing. The patient in these severe types naturally emaciates, and there is often fever due to secondary infections. There also may be dysphagia, vomiting, and diarrhea. The urine may even be blackish and frequently contains bismuth. Occasionally albumin and casts are present. These symptoms are produced by a pure bismuth salt. They are not the result of impurities, such as lead, arsenic, or antimony.

The Cause of the Poisoning. Our views in regard to the toxicity of the bismuth preparations have undergone a marked change since von Bardeleben wrote, in 1892, that of one thing we were sure; that was that even applications of magisterium bismuthi to large raw surfaces would not cause symptoms of poisoning unless the preparation were impure. Since then, and even before then (Kocher), there have been numerous reports of poisoning by bismuth until a fatal case reported in 1906 by Benneke and Hoffman[16] in a child, aged three weeks, to whom bismuth subnitrate had been given for *x*-ray examination, and a fatal case reported by Böhme,[17] in 1907, led Böhme to investigate the subject carefully. His results have already been outlined.

Since then others, among whom are Novak and Gutig,[18] Meyer,[19] E. G. Beck,[20] and Zabel,[21] have reported cases, some fatal, some showing marked collapse with recovery, in which methemaglobin was shown to be present in the blood in some cases. These authors are firm in their belief that the splitting of the subnitrate into nitrites is responsible for the toxic effects and they call it nitrite poisoning. Beck goes so far as to say that the line on the gums is a good sign. He has injected 720 grams (!) of 33 per cent. paste into the pleural cavity. Symptoms of poisoning set in and he removed the paste. Recovery followed.

Schumm[22] and Lorey[23] have been able to demonstrate frequently methemaglobin by means of the spectroscope in the blood of

[16] Münch. med. Woch., 1906, liii, 945.
[17] Loc. cit.
[18] Berlin. klin. Woch., 1908, xlv, 1764 to 1768.
[19] Therapeutische Monatshefte, 1908, xxii, 388 to 390.
[20] Jour. Amer. Med. Assoc., 1909, lii, 14 to 18; Zentralbl. f. Chir., 1910, xxxvii, 601 to 606.
[21] Deutsch. med. Woch., 1909, xxxv, 200.
[22] Ibid., 1910, xxxvi, 1250.
[23] Ibid.

those taking large doses of bismuth subnitrate, a fact not until then known. None could be found with therapeutic doses of the subnitrate and none could be demonstrated when large doses of bismuth carbonate or oxychlorate were administered. They deny the contention of Lewin that bismuth subnitrate poisoning is due only to the bismuth.

On the contrary, there is considerable experimental work with various bismuth salts in which the symptoms have been practically similar. Thus ammoniate citrate of bismuth (Feder-Meyer,[24] Mory[25]), subnitrate (Dalché and Villejean[26]), bismuth sodium tartrate (Mayser)[27], bismuth oxide and bismuth carbonate (Steinfeld and Meyer[28]) have been shown to produce acute or chronic poisoning in animals. Dermatol and Airol have produced symptoms of bismuth poisoning (Glaser,[29] Weissmüller,[30] Aemmer,[31] Stoeckel).[32]

Lewin[33] holds that all the symptoms, line on gums, ulceration, malaise, diarrhea, nephritis, collapse, are produced by metallic bismuth and have nothing in common with nitrite poisoning. He says that only a marked and easily demonstrable presence during life of methemaglobin in the blood can cause illness or death. All the preparations of bismuth are toxic.

Dalché and Villejean[34] called attention to the similarity in the toxic effects of lead, mercury, and bismuth. It is generally believed that a lead line on the gums is a sign of poisoning by lead; that spongy gums, stomatitis, and salivation indicate poisoning by mercury, then why do not a violet-black line on the gums, salivation and ulceration indicate poisoning by bismuth? It may be, and probably is, true that in certain cases of so-called bismuth poisoning following the administration of enormous single doses of bismuth subnitrate when there was inflammatory disease of the digestive tract, and when there was methemaglobinemia and death, the poisoning was due to nitrites. There is too much experimental and clinical evidence showing that it is the bismuth itself which is the poisonous agent, to allow us to accept unreservedly the idea that all the symptoms in all the fatal cases are due to nitrite poisoning. All the fatal cases reported in which methemaglobinemia was present occurred either in weakly infants the subjects of gastro-intestinal disorders, or in adults in whom there was inflammatory disease of the digestive tract.

A substance which is capable of causing the appearance of albumin and casts in the urine and which experimentally has produced glomerulonephritis, cannot be innocuous.

[24] Loc. cit.
[25] Loc. cit.
[26] Loc. cit.
[27] Loc. cit.
[28] Berlin. klin. Woch., 1892, p. 1024.
[29] Loc. cit
[30] Ibid., 1891, p. 1201.
[31] Schweizer Correspondensbl., 1897, p. 187.
[32] Münch. med. Woch., 1909, lvi, 643 to 645.
[33] Quoted by Dreesmann.
[34] Loc. cit.

General Comment. In the literature there are reports of more than 20 deaths caused by the administrations of bismuth preparations internally or as dressings for large raw wounds (burns particularly). There are numbers of cases of moderately severe poisoning such as the case reported in this paper. Verbal and written communications to me show that there must be many cases of rather severe poisoning following the use of Beck's paste which are not reported in the literature.

Beck naturally defends his paste, and in several articles has stated his conviction that the toxic effects are the result of nitrite poisoning. His position does not seem to be tenable in view of the weight of evidence that bismuth itself is at times quite toxic to the human organism.

It seems to be established from the data collected that the indiscriminate use of bismuth subnitrate in sinuses or in the intestinal canal is not devoid of danger. It would appear that one should take care that the paste in sinuses is gradually extruded. Should it remain deep in the sinus, it should be removed after a few days. In using it for *x*-ray work in the intestines, it appears best to withhold it in inflammatory cases or in cases where patients are much run down in health.

Substitutes such as carbonate of bismuth and oxide of iron, Fe_2O_3, have been recommended and are now being extensively used. The latter is highly recommended (Alexander,[35] Taege,[36] etc.).

In conclusion, it would seem that bismuth salts, like lead and mercury salts, may cause definite and characteristic symptoms of poisoning in more or less susceptible persons. Peculiarly characteristic of bismuth stomatitis is the whitish diphtheritic membrane which caps the ulcers. The visceral lesions caused by bismuth also show that it is one of the metallic poisons and therefore, should be used with caution.

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WEIGHT CURVES IN TYPHOID FEVER.[1]

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While there can be little doubt that under the ancient doctrine of "stuff a cold and starve a fever," loss of weight in the continued fevers was even greater than it is today, I shall confine the present discussion to the period during which typhoid fever has been recognized as a distinct disease—that is since 1837, when Gerhard and Pennock[2] finally established its differentiation from typhus fever. From that time to the present emaciation has been considered a characteristic symptom of the disease. It occurs in greater or less degree in all or nearly all cases. It is prominently mentioned in all complete descriptions of the disease, and has been regarded as a deplorable but necessary consequence of the infection. According to Loomis:[3] "Emaciation is perhaps more marked and rapid in this than in any other form of fever. It commences early and is progressive. By the time a patient has reached the fourth week of a typhoid of even moderate severity, he is usually in a condition of extreme emaciation." On the other hand, while admitting the occurrence of extreme grades of emaciation, Curschmann thinks that the losses in typhoid fever are not so great as would be anticipated, if one considers the duration of the disease and the extent of the losses in other infections.

Comparatively early in the history of typhoid fever exact observations were made upon the extent of the loss in weight. Yet in view of the fact that the majority of authors do not record the amount of food taken, it is difficult to compare their results. In a few instances, however, they have either plotted out the weight curves or have furnished data from which such curves could be constructed.

The following general summary represents, I believe, the most important results of all previous investigations:

Loss of weight occurs in practically all cases of typhoid fever but varies greatly in extent.

The severer the infection and the longer the duration of the disease, the greater the total loss.

The greatest loss observed by Curschmann[4] at the beginning of convalescence was 41 per cent. of the body weight. Scharlau[5]

[1] Presented in abstract before the Association of American Physicians at the Twenty seventh Annual Meeting, held at Atlantic City, May 15, 1912.

[2] Amer. Jour. Med. Sci., 1837, xix and xx. [3] Practical Medicine, 1892, 8th ed., 670.

[4] Nothnagel's Encyclopedia of Practical Medicine, 1905, Amer. ed., 368.

[5] Theoretisch-practische Abhandl. über den Typhus, etc. 1853.

had previously recorded a loss of 30 per cent. Losses of 19 per cent. in severe, and 10 per cent in mild, cases are common (Curschmann). On the other hand, the losses may be relatively insignificant, 1.5 per cent. to 3 per cent. in severe and 1 per cent. to 1.1 per cent. in mild cases (Curschmann.)

Daily losses of 300 to 500 grams are common; they may reach 1500 grams (Botkin[6]); and in a case complicated by parotiditis the loss amounted to 2500 grams in one day (Lorain[7]).

Lorain states that the maximum loss is reached at the end of the second or beginning of the third week, while according to Curschmann it is reached more frequently in the third than in the second week.

Kohlschütter[8] found that, after the more active period of the disease is over, the losses diminish with each week up to complete defervescence. Puritz[9] observed a corresponding diminution in the elimination of nitrogen.

Complications increase the loss of weight (Lorain, Cohin[10]).

While loss of weight usually ends with the return of the temperature to normal, it may extend far into convalescence (Leyden[11]), according to Curschmann to the third week. Curschmann has observed a loss of four pounds in the first week of convalescence.

All patients gain weight in convalescence, some rapidly, apparently without much, if any, increase in the quantity of food.

Contrary to the conclusions of the majority of observers, Garnier and Sabaréanu[12] found in their cases that the weight remained stationary, or increased a little, during the active febrile period; it diminished rapidly at defervescence; and in the afebrile period, remained unchanged until the patient began to take more food, when it increased. They attribute the course of the curve to the retention of water, and its sudden elimination.

Figs. 1 and 2 are taken from Puritz and Lorain. They illustrate the main features of the summary. Puritz's patient received a relatively full diet, taking an average of 160 grams of protein, 60 to 90 grams of fat, and 300 grams of carbohydrate a day. Lorain's patient received only a few spoonsful of milk.

The loss of weight in typhoid fever has been attributed to three factors: (1) Partial starvation; (2) the febrile temperature; and (3) the toxic destruction of protein.

1. *Partial Starvation.* Apparently at all periods in the history of typhoid fever it has been recognized that patients suffering

[6] Med. Klin. in demonstrativen Vortragen, Berlin, 1867, French translation, Paris, 1872, de la fiévre.

[7] De la temp. du corps humain et ses variations, etc., Paris, 1877-79 ii, 128 et seq.

[8] Volkmann's Sammlung inn. Med., 1887, No. 103 (No 303). p. 2773.

[9] Virchow's Arch. f. path. Anat., 1893 cxxxi, 327.

[10] Bull. gén. d. ther., 1887, cxii, 397.

[11] Deutsch. Arch. f. klin. Med., 1869, v, 366.

[12] Bull. Méd., 1908, xxii, 999.

from the disease were undernourished. Bretonneau[13] characterized their condition by the term *autophagia*. Graves,[14] Trousseau,[15] Chudnowsky,[16] Flint,[17] Barrs,[18] and Shattuck[19] insisted, in their respective periods, that typhoid fever patients were undernourished, and introduced diets of greater nutritive value.

Proof of the influence of partial starvation upon the loss of weight occurring during the disease is furnished by the observations of Puritz, von Leyden and Klemperer,[20] and others who succeeded in diminishing the loss by increasing the intake of food. Recently it has been found possible to maintain many patients in weight equilibrium by administering sufficient food.

FIG. 1.—Showing influence of complication on weight. Patient received only a few spoonsful of milk a day.

2. *The Febrile Temperature.* The effects of an artificially raised temperature (through hot baths, heated air, or injury to the heat centres) upon protein metabolism are comparatively well known. It is probable, but has not been proved, that fat and carbohydrate metabolism are similarly affected. Temperatures under 39° C. cause only slight increase in protein destruction; temperatures over 39° C. likewise have but little effect unless they are prolonged for more than three hours; artificial heating for twelve hours has caused an increase in protein destruction amounting to 37 per cent. (F. Voit).[21]

These results apparently confirm the clinical observation that intermittent temperatures are not, as a rule, attended by such

[13] Cited by Trousseau, Clinique Médicale, Paris, 1872, 4th ed., i, 353.
[14] Clinical Medicine, New Sydenham Society, 1884, i, 136
[15] Clinique Médicale, Paris, 1873, 4th ed., i, 350.
[16] Cited by Puritz.
[17] Practice of Medicine.
[18] British Med. Jour., 1897, i,125.
[19] Jour. Amer. Med. Assoc., 1897, xxix, 51.
[20] Von Leyden's Handb. d. Ernährungs-Therapie, 1904, 2d ed., p. 332 et seq.
[21] Sitzungsberichte c. Gesellschaft f. Morph. u. Physiologie in München, 1895, xi, 120.

marked loss of weight as those which are continuous. They also suggest that the diminished loss in the later stages of typhoid

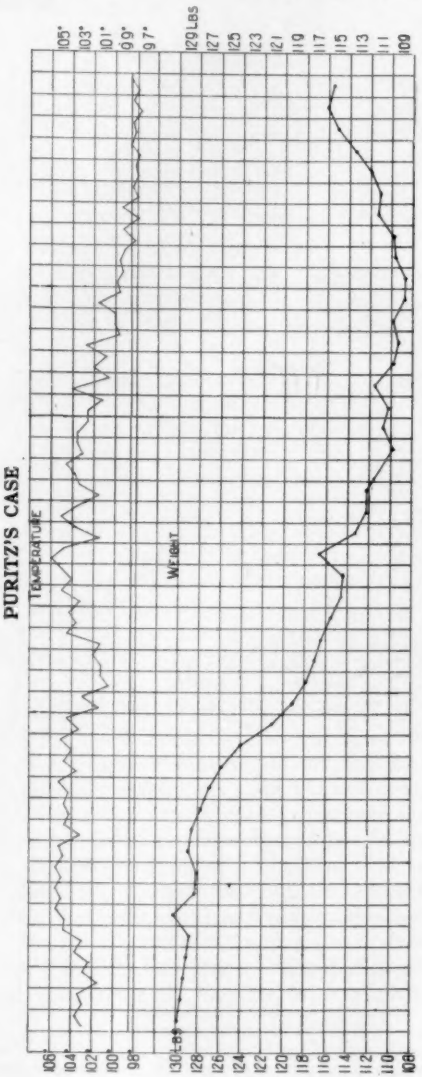

FIG. 2.—Patient received an average of 2600 calories a day.

fever may be due in part to the change in character of the temperature curve.

3. *Toxic Destruction of Protein.* The loss of nitrogen in the infective fevers is greater than occurs in a healthy man who is starved, or, according to the common belief, than can be accounted for by the pyrexia itself. Upon this basis it has been assumed that the toxins of the infecting microörganism exert directly a destructive influence upon the cells of the body.

Whether the theory, in its generally accepted form, is correct or not does not concern us at this time. It has been proved possbile to bring a patient suffering from typhoid fever into nitrogen and weight equilibrium by the exhibition of a diet containing a large amount of carbohydrate, and a relatively small amount of protein.

WATER-RETENTION THEORY. The discussion of weight curves in typhoid fever would not be complete without reference to the theory of water retention. This theory must be considered from two standpoints: (1) The influence of the disease itself, and (2) the influence of a diet containing a large amount of carbohydrate.

1. *The Influence of the Disease.* The water balance has not been thoroughly investigated for any fever, and conflicting opinions are held concerning it in typhoid fever.

Leyden was one of the first to refer to the theory of water retention. The sudden losses of weight which have been observed with remissions of temperature, especially toward the end of the febrile period, probably indicate that water is retained in some cases. Yet Krauss[22] speaks of the "alleged retention of water in fever" as pure "conjecture." Stähelin's[23] dog, infected with surra, eliminated more water than he ingested. Schwenkenbecher and Inagaki[24] conclude from their experiments that water is not retained in the body in fever,

On the other hand, Garnier and Sabaréanu[25] believe that retention of water occurs during the febrile stage of typhoid fever and that this is responsible for the supposed maintenance of weight during this period.

In view of the conflicting opinions and the absence of conclusive studies of the water balance, the question of water retention in fever due to the disease itself must be left open for the present.

2. *The Influence of a Diet Rich in Carbohydrate.* The increasing use of diets rich in carbohydrate in typhoid fever renders it important to determine whether such a diet is likely to cause retention of water in the body. As is well known, a poorly balanced diet may cause variations in the excretion of water. For example, in an experiment conducted by Benedict and Milner,[26] it was found that water was retained on the first of three days when the subject was confined to a diet consisting of 965 to 969 grams of carbo-

[22] Von Noorden's Metabolism and Practical Medicine, Chicago, 1907, ii, 139.
[23] Arch. f. Hygiene, 1904, l, 77.
[24] Arch. f. Exp. Path u. Pharm., 1906, liv, 168. [25] Loc. cit.
[26] United States Department of Agriculture, Experimental Stations Bulletin, No. 175, 1903-4, p, 226.

hydrate; on a diet of 745 to 750 grams of fat, water was lost during the whole period. It is generally agreed, however, that a well proportioned diet does not affect the water balance.

While the proportion of the foodstuffs in the diet which we employ varies necessarily with different patients, and in some instances has been subject to sudden experimental changes, there has been no constant relation between variation in weight and the quantity of urine. Though water may have been retained by some patients, and have caused an increase in weight, there has been no clinical reason to think that such was the case. There has been no visible edema, and patients have not lost weight suddenly, following diuresis, when the amount of carbohydrate in the diet was diminished during convalescence.

In addition to the above considerations, we now possess evidence that at least a part of the gain in weight in the late stage of the febrile priod and in convalescence is due to the conversion of dextrose into fat. In one instance, 38 per cent. of the carbohydrate metabolized during the period of observation (fifteen minutes) was so transformed.[27]

The distribution of the losses among the various tissues of the body requires brief consideration.

It appears probable that all of the tissues share in the losses, though to what relative extents can only be surmised at present. The increased elimination of nitrogen in patients who are undernourished, forms the basis for the assumption that the muscles suffer marked loss. Loss of fat, as well as of muscle, is evident clinically in severe cases.

With the aid of a respiration chamber, Grafe[28] studied the respiratory quotients of typhoid fever patients in the fasting state, and reached the conclusion that the metabolic processes follow normal laws, though with increased intensity. Rolly's[29] studies on the respiratory quotients of patients from four to six hours after food, and our own studies in Bellevue Hospital upon patients taking a full diet, lead to the same conclusion. If these results are ultimatly confirmed, the consumption of the body tissues in typhoid fever, when the patients are undernourished, proceeds in the same manner as in healthy persons who are partially or completely starved. The stores of glycogen are depleted first—probably within a few hours when the fever is high and, at most, within a few days—after which fat and protein constitute the sole sources of the body's energy. The duration of life in a healthy animal which is starved is measured by the amount of fat which the body contained at the start (Lusk).[30] The often noted fact

[27] Unpublished observations upon the respiratory exchanges carried out with the assistance of Dr. E. F. Du Bois.

[28] Deutsch. Arch. f. klin. Med., 1910, ci, 209.

[29] Ibid., 1911, ciii, 93.

[30] Science of Nutrition, 1906, p. 65.

that obese patients do not bear typhoid fever well does not come into consideration here, since the causes of this fact can only be conjectured. Another analogy of the processes of metabolism in typhoid fever to those in starvation must be noted: in partial or complete starvation the body begins, after a time, to economize its available energy by reducing its total metabolism. A similar economy of energy has frequently been observed in typhoid fever. Moos[31] found as long ago as 1855 that the nitrogen losses diminished in the later weeks of the disease. Kohlschütter[32] emphasized his observations that the loss of weight diminishes with each week after the more active period of the disease is past. Cohin[33] called attention to the same fact. This is the probable explanation of the continuance of life in patients who take a wholly inadequate amount of food and yet live from week to week with high fever.

Influence of the High-calory Diet upon Weight. My own observations upon the weight curve in typhoid fever were begun in 1908. A satisfactory balance could not be obtained upon the market so I had the hospital carpenter construct a wooden table which would rest upon the platform of the ordinary hospital scales. When in position, the table is the same height as the bed, and the weight of a patient may be taken without more disturbance than shifting his position in bed—with much less exertion, in fact, than is required to administer a tub bath.

Weights have been taken of practically all patients, usually every second or third day. The procedure was adopted originally for the purpose of having additional clinical control upon the effects of the diet. Slight sources of error enter into the observations, which are clearly recognized, but which so far it has been impossible to eliminate.[34] While such errors may, and probably do, affect the relation of one day's weight to another, apparently they do not affect the general trend of the curve. The errors referred to are: Patients have not always been weighed at the same hour of the day, or with regard to whether they have recently been fed or have urinated. The morning defecations do not come into consideration as the weights have never been taken before the administration of the daily enema. The clothing of the patients, however, has always been carefully considered. In future observations, it is hoped that these sources of error may be eliminated.

The figures which follow, with the exception of Fig. 3, illustrate the influence of a full diet upon the weights of patients during the febrile period, convalescence, and relapses. The curves are typical of the effects of the diet. Fig. 3 is the curve of one of the earlier patients of the series, to whom it was impossible, with our

[31] Zeitschr. f. rationelle Med., N. F., No. 7, 1855.

[32] Loc. cit.

[33] Loc. cit.

[34] The weights have been taken by various members of the interne staff after the general demands of the wards have been attended to.

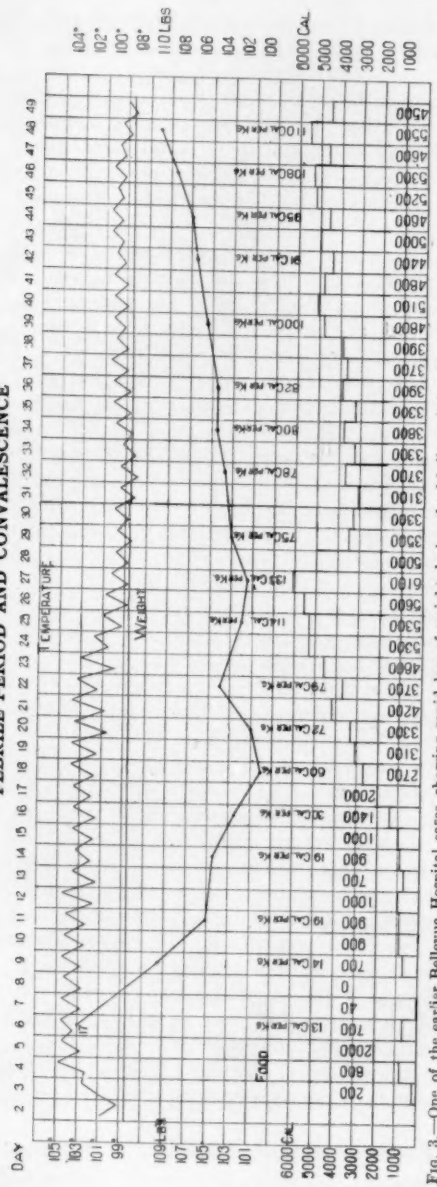

FIG. 3.—One of the earlier Bellevue Hospital cases, showing rapid loss of weight during the febrile period, when the amount of food was insufficient, and the gain in weight in convalescence.

then limited experience, to give the amount of food required until toward the end of the febrile stage. The general course of the curve is similar to those obtained by the earlier investigators.

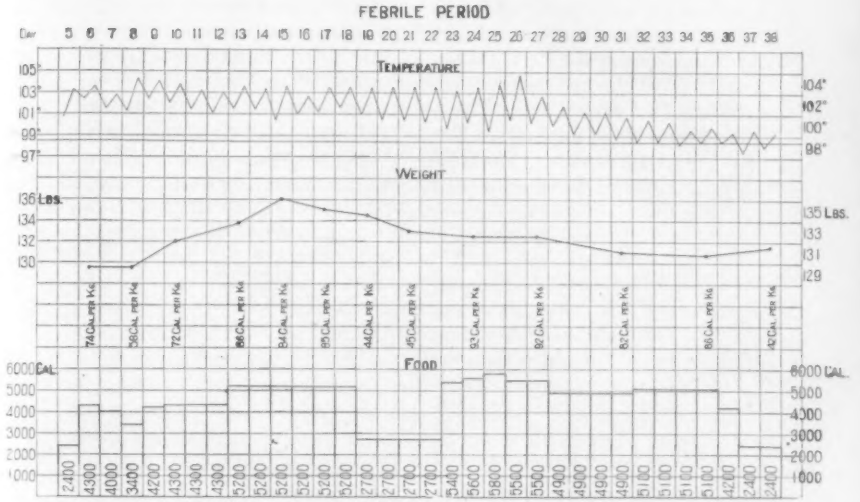

Fig. 4.—Showing that weight equilibrium may be maintained by sufficient food.

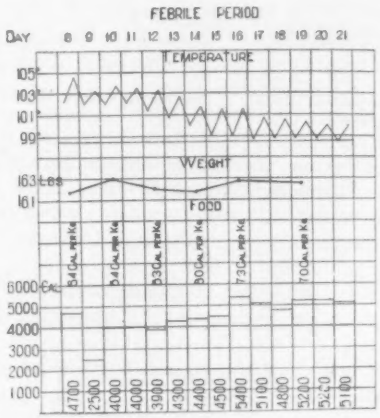

Fig. 5.—Showing the maintenance of weight equilibrium.

There is no evidence in the curve of water retention either during the febrile period or in convalescence.

The gains in weight during relapses and in convalescence are

less noteworthy than the maintenance of weight during the active stages of the fever.

The ability of the body to repair its losses after wasting diseases is nowhere better shown than in convalescence from typhoid fever. This fact has been known for many years. Botkin stated that such patients gained weight rapidly at first, more slowly later. According to Liebermeister,[35] patients may gain as much as five to seven pounds a week, according to Schottmüller,[36] as much as eleven pounds. In Puritz's cases, the weight remained stationary for the first two or three days after the temperature reached normal and then began to increase. Fr. Müller[37] found that patients convalescing from typhoid fever are able to retain nitrogen on a diet which

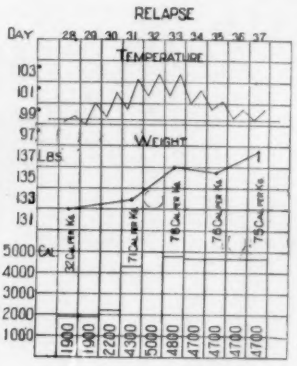

FIG. 6.—Showing an increase in weight during a relapse.

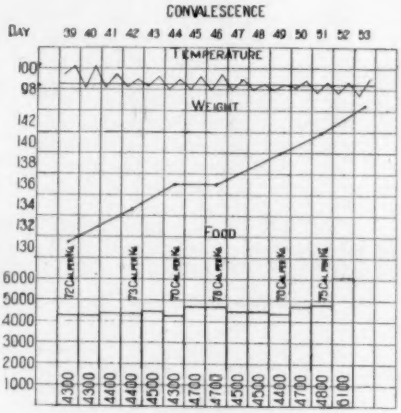

FIG. 7.—Showing rapid gain in weight during convalescence.

with its low fuel value is insufficient to maintain nitrogen equilibrium in health. He reports a case which retained from the third to the tenth day of convalescence a daily average of 1.3 grams of nitrogen on a diet furnishing only 1165 calories and 9.9 grams of food nitrogen.

As is illustrated in Fig. 3, patients who have lost much weight during the febrile stage may repair the damage before they are able to get out of bed.

In one of Puritz's cases the weight remained stationary during a relapse of sixteen days' duration.

CONCLUSION. It is possible to maintain patients suffering from typhoid fever in weight equilibrium throughout the entire course of the disease by giving them sufficient food.

[35] Ziemssen's Cyclopedia of the Practice of Medicine, Wood, 1874, i, 95.
[36] Mohr and Stähelin's Handb. d. inn. Med., 1911, i, 483.
[37] Zeitschr. f. klin. Med., 1889, xvi, 542.

OBSERVATIONS UPON SCARLET FEVER, DIPHTHERIA, AND MEASLES AT THE CINCINNATI CONTAGIOUS HOSPITAL.

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Although there are numbers of good men who, patiently and perseveringly, are working in their laboratories and wards upon the problems which our contagious diseases present, and the results of their efforts appear at intervals, one is impressed with the comparatively little written upon the subject. I refer in this paper only to scarlet fever, diphtheria, and measles. This may be due to a placid conclusion on the part of many that our text-books have settled the clinical signs and symptoms and that repeated failures along etiological and bacteriological lines yield little of promise for the future. This I think is incorrect and some one's persistent efforts will eventually be crowned with success.

Scarlet fever appears variously disguised, probably more so than any other contagious disease, and if we can find out practically for ourselves that we have in the past laid too much stress upon certain so-called classical signs and not enough upon others and that a rearrangement of some of our ideas seems advisable, we may be helped to an earlier recognition and, therefore, a more prompt isolation and treatment of this affection. During the last year in the contagious hospital we have had an excellent opportunity for studying this disease especially, and it is my desire to furnish statistics as we found them in this and the other diseases, with certain observations which were made concerning clinical manifestations, laboratory findings, and treatment.

Observations were made upon over 300 cases of scarlet fever. The following summary indicates in percentage form our findings in the so-called classical symptoms and diagnostic signs:

Scarlet fever, 315 cases. Onset with vomiting, 50 per cent.; onset with headache, 4 per cent.; onset with sore throat, 65 per cent.; eruption, whole body, 46 per cent.; eruption, partial, 35 per cent.; mouth pallor, 57 per cent.; rash on soft palate, 38.6 per cent.; membrane on tonsils, 29 per cent.; papillæ enlarged, 56 per cent.; glazed tongue, 17.7 per cent.; anterior cervical glands enlarged, 95 per cent.; submaxillary glands enlarged, 72 per cent.; eruption gone from body, five and one-half days; desquamation began in six and three-quarter days; blood count, leukocytes average, 17,000; polymorphonuclears, average, 78 per cent.; large lymphocytes, average, 6.3 per cent.; small lymphocytes, average, 10.1 per cent.; eosinophiles, average, 2 per cent.; albumin, 11 per cent.; granular casts, 4 per cent.; hyaline casts, 2.5 per cent.; blood cells, 4 per cent.; myocarditis, 6 per cent.; irregular heart,

3 per cent.; murmurs, 8 per cent.; mastoiditis (no facial palsy in this series), 1 per cent.; arthralgia (all cases had immunizing doses of diphtheria antitoxin), 6 per cent.; acetone, 49.5 per cent.; diacetic acid, 22.6 per cent.; indican, 73 per cent.; temperature gone in five and two-third days; nephritis, 2 per cent. The average white count of cases which died was 17,262. Preponderance of the staphylococcus may have influenced all leukocyte counts.

Concerning the above summary a few comments seem pertinent: Onset with vomiting occurred in only 50 per cent. of our cases which is rather disappointing, as so much stress has always been laid upon this sign. McCullom[1] says that it occurred in 80 per cent. of his cases, but Welch and Schamberg give their figures also as 50 per cent., and add that they consider this rather lower than usual. I think that this is a just criticism and that in most epidemics the figures would be considerably higher.

We observed mouth pallor in 57 per cent. which is also lower than we would expect. No statistics were obtainable from other sources in regard to this, McCullom merely says that it occurs constantly in moderately severe cases. It has been our experience that the rash occurs on the face in only a small number of the cases, but when this is present or if there is only a febrile blush upon the cheeks, the skin around the mouth and nose remains exempt. When this is seen I believe it to be quite characteristic.

Thirty-eight and six-tenths per cent. had rashes upon the soft palate and fauces and where this is present, namely, a generalized blush, punctate in character, I believe it to be our most important diagnostic sign.

The papillæ appeared enlarged in 56 per cent. of our cases. Concerning this McCullom says that the condition is constant, but may be missed at times, and Welch and Schamberg say that it may or may not be present in mild cases. When present, even with the glazed tongue (17.7 per cent.), it is not absolutely pathognomonic, as it may occur in certain forms of gastro-intestinal disturbance in which there is not the slightest suspicion of scarlet fever. The strawberry tongue, however, taken together with a generalized blush, punctate in character, upon the soft palate and fauces, need leave very little doubt as to the character of the disease.

I think these two symptoms are very much more significant than an apparently characteristic rash upon the body. We have tried to emphasize the importance of laying more stress upon the mouth symptoms and not depending upon the body rash. However, the whole picture should be considered.

Our average white count was 17,000. The maximum was 38,000. The text-books lead us to expect a uniformly higher count than

[1] Osler's Modern Medicine.

this. We felt that a satisfactory one was between 20,000 and 35,000. Kotschetkoff and Bowi's[2] figures are between 10,000 and 40,000, Rieder's 40,000, Felsenthal between 18,000 and 30,000, and Tileston between 18,000 and 40,000.

The average polymorphonuclear count was 78 per cent. Kotschetkoff gives between 85 and 98 per cent.

The low percentage of eosinophiles, 2 per cent., was probably due to the fact that the blood counts were made early in the disease.

McCullom observed albumin in 72 per cent. of his cases at the South Department, while Roger reports 38 per cent. Our cases showed the presence of albumin in only 11 per cent. I believe that a practical reason for this may be found in our routine treatment. All cases were confined to bed for at least three weeks and kept upon a strictly milk diet until their temperatures were normal for seven days. Eggs and broths were withheld until the fifth week and red meats until the latter part of the sixth. Of equal importance with this is the systematic giving of large quantities of water from the time of their admission to the hospital. At first potassium citrate was ordered, more or less as a placebo, to be given hourly or two hourly in water, with the idea that the patients would get the fluid more religiously if medicine were ordered with it. How much restraining influence the alkalinizing power of this drug exerted upon the presence or absence of albumin in the urine we will consider later.

In our estimate of nephritis we included all cases showing the presence of albumin, casts, and red blood cells, and this we found to be only 2 per cent. Welch and Schamberg[3] quote Vogl as reporting 34 per cent. of nephritis in his cases, Cadet de Gassicourt, 30 per cent., Baginsky, 9.57 per cent., Caiger, 3.32 per cent., and Holt gives as his figures between 6 and 10 per cent.

Let me call attention to the fact that about 50 per cent. showed the presence of acetone in the urine; less than half that number showed diacetic acid, and almost 75 per cent. reacted for indican.

Practically all the cases desquamated, although some very slightly.

None of our scarlet fever cases contracted diphtheria in the house, although 2 or 3 showed the presence of the Klebs-Loeffler bacillus upon admission. The most susceptible period for this disease is the third, fourth, and fifth week. Variat and Deve report 30 cases positive for the Klebs-Loeffler bacillus in 525 scarlet fever patients; Garret and Washburn,[4] London Fever Hospital, report 1 per cent.; Welch and Schamberg,[5] Municipal Hospital in Philadelphia, found between 19 and 32 per cent. positive. Some allowance should be made for the method employed

[2] Quoted by Welch and Schamberg.
[3] Ibid.
[4] Ibid.
[5] Ibid.

in reporting the presence or absence of the Klebs-Loeffler. We used the Westbrook classification entirely, which is liberal and will be referred to under diphtheria. At least four cultures were taken from the noses and throats of all scarlet fever patients.

The so-called Pastias sign in this disease, namely, the accentuation of the rash in the normal folds, especially on the anterior surface of the elbow, has not been noticed except in a few instances, so that no significance has been attached to it.

Of like importance is the Rumpel-Leeds phenomenon or the hemorrhages at the elbow from compression of the upper arm by means of a bandage. Observations made by others have shown it to occur with equal frequency in measles and in normal children.

In taking up the treatment of special conditions we may first refer briefly to the subject of immunization against scarlet fever. We have had practically no personal experience with this line of work, except to give one light case which was exposed to the most virulent form of the disease one million killed streptococci taken from scarlet fever patients (a vaccine which was on the market) and which case continued to have a mild attack, and another, a very malignant case, five daily doses from 500,000 to 4,000,000 of the same scarlet fever vaccine. This patient's condition was uninfluenced by the treatment and the patient died in a few days. The above should come under the heading of treatment of the disease rather than immunization. If there is any close connection between the streptococcus and the virus of scarlet fever we would look for our best results from an antistreptococcus serum, made from scarlet fever patients rather than a vaccine, as the former (the serum) already contains the antibodies and should act more promptly, while the latter (the vaccine) simply helps the patient to form his own. The field for the vaccine is in immunization.

With the use of the ordinary antistreptococcic serum made up of streptococci not from scarlet fever patients we have noticed little benefit even in doses of 80 or 90 c.c. in twenty-four or thirty-six hours. If it is used at all it should be made from the streptococci from blood, throat, or glands of scarlet fever cases. Such a serum has been hard for us to obtain from any source, because of the difficulty we have experienced in isolating streptococci from our cases.

Federinski in Moscow (1910), in an analysis of 317 cases which received the antistreptococcic serum (made from scarlet fever streptococci) says that it helps chances of recovery if given before the fifth day. His dosage was 200 c.c. to adults and 100 to 150 c.c. to children, repeated in twenty-four or forty-eight hours if necessary. Mathias Nicoll, New York (1910), reports only fair results. If obtainable, it should be used in some cases, in enormous doses always, for lack of something better, either subcutaneously

or intravenously, according to immediate needs. It might help minimize the complications.

Professor Schwenkenbecker, director of the Frankfurt Hospital Medical Clinic, recommends the injection intravenously, not later than the fourth day, of serum (healthy as to syphilis or tuberculosis and culturally sterile), taken from at least 3 (namely, a polyvalent serum) scarlet fever cases suffering from a severe but uncomplicated type of the disease in late convalescence. Treatment with this sera should cease not later than the eighteenth to the twenty-fourth day from the onset. The dose should be 40 c.c. for children and 100 c.c. for adults, and doses may be given at intervals of from one to seven days according to the severity of the case. He suggests that only the severe and unquestioned cases of scarlet fever be injected.

Karl K. Koessler and Jessie M. Koessler,[6] in experiments concerning specific antibodies in scarlet fever concluded that "the serum of scarlet fever patients contains specific antibodies for an unknown virus which seems to be present especially in the cervical lymph glands." Personally, I think that we should direct our efforts toward discovering a specific serum for the treatment of this disease to the preparation of sera derived from the blood stream or, more probably, from the cervical lymph glands of scarlet fever patients, rather than to vaccines or serums containing the streptococcus or its antibodies.

Out of 50 or more nurses who have been on duty in the wards, 3 (about 6 per cent.) contracted the disease in the house, while none of the internes did.

W. H. Waters, of Boston, reports results in immunization against scarlet fever, of nurses on contagious duty. He used different strains of streptococci, killed and standardized in usual way, taken from throats of scarlet fever patients. For two or three weeks before going on duty the nurses received three immunizing doses, of 50,000,000, 100,000,000, and 200,000,000 organisms of a polyvalent vaccine. Of those receiving the vaccine, 2.7 per cent. contracted the disease and of those not receiving it 35.7 per cent. contracted it. These figures are rather amazing as his nurses must have been unusually susceptible.

Kolmer, of Philadelphia, in trying to raise the streptococcoopsonic index, found experimentally that he was able to do so slightly, but concluded that it was so slight as to make the likelihood of establishing an immunity against streptococcic infection very dubious. Again, in experimental studies on streptococcus antibodies with special reference to complement fixation reactions, he concludes that a streptococcus produces a specific antibody up to a certain limit, but "finding but 11.2 per cent. of positive

[6] Jour. Infect. Dis., November, 1911, vol. ix, No. 3.

reactions in scarlet fever tends to show that streptococcus infection in scarlet fever severe enough to produce immune bodies is not so common as is generally believed."

Nasal and ear discharges were reported promptly and a number of autogenous and stock vaccines (in all 10, an inconclusive number it is true) were prepared.

It is the opinion of most workers that stock vaccines give equally as good, if not better results than the autogenous, because the former can be administered much more promptly and several days are gained for the patient, a very important consideration. Our results with these vaccines were not brilliant. Cases using vaccines had no local treatment. Irrigations were employed for the others. Except in one or two instances we could not see that the discharge was in any way modified by the vaccine and on the whole, those having local treatments ran a shorter course. The dosage in each case was started with about 200,000 and each succeeding dose was doubled at intervals of from two to ten days according to indications. This was carried up to 128,000,000 in some cases. This method has so far been disappointing, but in the hands of Kolmer, of Philadelphia, good results have been reported. It is possible that in some instances our intervals of administration and dosage were faulty, yet the method is certainly in line with modern vaccine therapy in other directions. Many cases, however, having local treatments, where intelligently applied, yield results, which, if vaccines were being used, would be considered brilliant.

We have taken the opportunity in our wards of applying wherever feasible, the treatment for nephritis as suggested by Dr. Martin Henry Fischer.[7]

This therapy is based upon certain theories, or more correctly, facts, since they have been confirmed by laboratory experiments and as they are a departure from our formerly accepted views on nephritis, it may be well to briefly summarize a few details of his work and conclusions for the benefit of those who are not familiar with them. They are as follows:

It is assumed that nephritis is due to an acidosis in the kidney. Emphasis is laid upon the colloidal structure of the blood, both red and white corpuscles and the liquid portion, also that the urinary membrane, namely, everything between the urine and the blood, consists of various emulsion colloids in the solid state. Colloid material is also present in the urine normally, but is not visible as albumin to our ordinary tests.

The fluids and tissues of the body (except the gastric juice, urine, sweat, vaginal secretion, and alimentary contents, when fat is fed) are practically neutral in reaction. Normal blood is neutral in reaction, but contains both alkalies and acids.

[7] Nephritis.

An abnormal production or accumulation of acid in the kidney renders the colloidal urinary membrane soluble and permits a part of it to pass into the urine as albumin.

This has been demonstrated by experiments. Fibrin, an albuminous structure, when mixed and shaken with plain water (of neutral reaction) swells only slightly and the water shows no reaction for albumin. If hydrochloric acid is added there is greater swelling of the fibrin and albumin is present (by the precipitation of the fibrin) in the water in accordance with the amount of swelling. If sodium chloride or any other salt is mixed with the hydrochloric acid, less albumin goes into solution, the higher the concentration of the salt. Gelatin (another colloid) acts practically the same way as fibrin.

A high alkali content can as readily put the colloids, fibrin, and gelatin into solution (namely, dissolve the albumin) as can an acid. This is probably no factor in the production of a nephritis as the normal CO_2 production in the living cells tends quickly to neutralize it.

Fischer found that by injecting acid into the ear of a rabbit, its normally alkaline urine became acid. Albumin, casts, epithelial cells, blood corpuscles, and hemoglobin appeared promptly in the urine which was also diminished in quantity. Edema of the tissues was noticed as well.

An over supply of acid in the tissues in extreme muscular exertion and the severe anemias, without adequate oxidation, shows albumin in the urine.

Contrary to the views of many he holds that albuminuria is the constant accompaniment of salt starvation.

Actual experiments on the kidney by Fischer are in line with the preceding observations. He found that the structures of the kidney in the presence of an acid swell, take in water, and part of the colloid material is dissolved as albumin and precipitated as granules.

This brief summary suggests the "Fischer" treatment for nephritis, namely, an alkali, salt, and plenty of water.

It occurred to us that as the contagious diseases are frequently accompanied by an acidosis, as exemplified by the presence of acetone in about 50 per cent. of our cases and diacetic acid in 22.6 per cent., that the alkaline treatment might help to control the progress in the severe septic types of the disease. Apparently it exerted little or no influence in staying the course of the purely septic types which were unaccompanied by any special nephritis. Fischer says that he would not expect it to have any material influence upon that type of case. Sodium carbonate given by the mouth was not well tolerated as a rule, and seemed to be somewhat more irritating to the rectum than a normal salt solution. However, a large majority of the cases retained a sufficient amount

in that way. Potassium citrate was substituted when giving an alkali by mouth and has been given to all my cases hourly or two hourly, whether or not they had evidences of albumin or nephritis. Probably the low percentage of albuminurias (11 per cent.) and that of nephritis (2 per cent. in 388 cases of scarlet fever) observed in our wards is due to the routine alkaline "plenty of water" treatment, which all the cases have had. Their urine part of the time was alkaline and never highly acid.

Two cases present interesting features:

CASE I.—M. D., male, aged three years. Severe septic type with both ears discharging, profuse nasal discharge, enlarged glands, weak, irregular heart with bruit at apex, eyelids, and feet edematous. Urinalysis, albumin negative. Amount of urine very scanty, blood cells and hyaline casts. Started alkaline-salt solution per rectum. The solution contained sodium carbonate (crystals), 10, sodium chloride, 10, in 1000 c.c. of water. A half strength dilution of the above was used. Four ounces were given per rectum every three hours and were expelled occasionally. Potassium citrate, grains five in water, was given by mouth every one to three hours.

On the ninth day of the illness Fischer's solution was given intravenously. Same formula as above was used except that sodium chloride was increased to 14 in the 1000 c.c. of water and a half dilution given. Only 10 ounces were used as the patient showed signs of collapse. At least a pint and a half should have been given very slowly had we been able to do so. Next day one pint was given again intravenously. The amount of urine passed increased promptly, and the edema disappeared. Gradual improvement of general symptoms with complete recovery resulted.

CASE II.—J. D., male, aged four years. Light case of scarlet fever with temperature reaching normal on the fifth day. He passed from 8 to 33 ounces of urine daily up to the thirty-first day of the illness. On the twenty-seventh day (end of fourth week) the urinalysis showed: Specific gravity, 1010; albumin, a heavy trace; few coarse granular casts; red and white blood cells.

The child was somnolent and was aroused with difficulty. Vomited several times. Pulse varied between 90 and 122, with blood pressure high (systolic pressure sometimes reaching 144). The child seemed on the verge of uremic convulsions. There was puffiness of the face and eyelids and slight edema of the feet. There was no fluid in the serous cavities at any stage.

For thirteen days after the nephritis commenced, except once, albumin from a slight to a heavy trace was reported daily in twenty-four-hour specimens. It then disappeared not to return again.

During the presence of albumin, red and white cells were found in abundance. Casts were rare. An occasional granular, and a few blood casts were reported once and part of one cast another

time. There were no hyaline casts. After eight days the blood cells were few in number and gradually disappeared, to be entirely gone about the eighteenth day. The specific gravity varied between 1002 and 1028, usually between 1002 and 1010. The urine was reported as acid only twice after the fourth day. The amount of urine passed daily varied from 30 to 60 ounces.

TREATMENT. The treatment was as follows: For ten days after albumin was discovered the patient had sodium chloride, grains five, and potassium citrate, grains eight, by mouth in as much water as he would take every hour day and night. Fischer's solution, one-half dilution (of the sodium chloride 10, sodium carbonate, crystals, 10, water 1000 c.c. strength), ounces, five, per rectum was given at two hour intervals during the day and three hour intervals during night, and was retained. After ten days the intervals of administration both by mouth and rectum were lengthened.

During the period of high blood pressure, veratrum viridi, minims two, every three hours, was given during the day. Fischer's solution intravenously was not necessary.

Blaud's pills were started during convalescence as a tonic. During the attack the child showed a mild grade of anemia. The red blood cells were 4,600,000. Recovery was complete.

There were several interesting features about this case. He started with what appeared to be a terrific case of nephritis with the urine absolutely loaded with red blood cells and a large amount of albumin. One striking thing was the great scarcity of casts of all descriptions. How much this was influenced by keeping the urine absolutely alkaline, by the constant administration of salt, and the ingestion of large quantities of water is an interesting question. With the starting of the treatment all symptoms improved and continued to do so consistently.

We found that grains twelve to thirteen hourly of potassium citrate by mouth in the adult and grains five to seven in children, aged four to seven years, was sufficient to keep the urine alkaline.

As I have said before, nephritis has been of rather rare occurrence in our wards, but whenever tried the alkaline salt treatment has given satisfactory results.

True relapses or reinfections were not observed, but delayed rashes occurred in 1 or 2 instances.

Eighteen blood cultures were made during the year from scarlet fever patients. Of these 9 were negative. In the other 9 cases the Staphylococcus pyogenes aureus was recovered seven times and the albus twice. We were unable to recover the streptococcus from the blood.

The throat and nose cultures almost uniformly showed the presence of staphylococci, occasionally mixed with a few streptococci.

Atmospheric plate cultures (88 in number) in wards before fumigation showed the presence of the Staphylococcus aureus and albus, the Streptococcus pyogenes, but never the Klebs-Loeffler bacillus. After fumigation with formaldehyde, plate cultures were always negative.

Twelve cervical glands of scarlet fever patients were aspirated with aseptic precautions in an effort to corroborate the claims of Vipond made in the spring of 1911, that he had found the specific organism of scarlet fever in the glands of patients suffering from this disease. The cultures were sterile in 9 cases; the Staphylococcus pyogenes aureus was isolated twice and the pyoscyaneus once. Our results did not verify his findings. This has also been the experience of others. Experiments by Dr. Nicoll show that Vipond's bacillus was probably a contamination from the asbestos packing of his syringe.

The following summary shows observations made upon 76 cases of diphtheria:

Onset with sore throat, 84 per cent.; onset with vomiting, 33 per cent.; membrane on tonsils, 85 per cent.; membrane on soft palate, 36 per cent.; inflammatory swelling, 30 per cent.; membrane gone on the average in two and seven-elevenths days; temperature normal on the average in three and three-quarter days; erythema (not from serum), 5 per cent.; urticaria (not from serum), 14 per cent.; otitis, 5 per cent.; albumin, 12 per cent.; adenitis, 47 per cent.; paralysis, soft palate, 5 per cent.; paralysis of other muscles, 4 per cent.; myocarditis, 16 per cent.; endocarditis, 28 per cent.; slow pulse, 4 per cent.; arthralgia, 2.6 per cent.; acetone, 28.5 per cent.; diacetic acid, 14 per cent.; indican, 32 per cent.; serum rashes, 16 per cent.; antitoxin, average dose, 40,000 units, highest dose, 355,000 units; blood count: Leukocytes, average, 13,633.

Types of Klebs-Loeffler bacilli found in Wesbrook classification: C, 58 per cent.; D, 39 per cent.; A, 22 per cent.; E, 8 per cent.; E_2 and F_2, 5 per cent.; B, D_2, and F_1, 3 per cent. Other solid forms occurred less frequently.

Glancing at the table we see that vomiting occurred at the onset in only 18 per cent. of the cases while in scarlet fever the percentage was 50.

A striking feature about the table is that the average dose of antitoxin was 40,000 units. This is accounted for by the fact that a number of desperate cases, having been sick about a week before admission, required enormous doses which brought up the average considerably. Many required only small doses. Our rule was to give from 2000 or 3000 to 12,000 units from two to three times in twenty-four hours, until signs of improvement were noticed.

A husband and wife, sick one week before admission, came in completely overwhelmed by the disease. The former had the

pharyngeal type, his pharynx being completely covered by a membrane about one-eighth of an inch thick. He had the record dose, 355,000 units. He developed some arrhythmia, but showed no serum rashes or arthralgia. He was in an advanced stage of tuberculosis before acquiring diphtheria and died from that disease later. His wife had a bad laryngeal type of diphtheria, with pronounced stenosis, loss of voice, and extreme prostration. She received 345,000 units and made a complete recovery, without serum rashes, arthralgia, evidences of myocarditis, or any other complication. Advanced laryngeal cases received antitoxin unsparingly.

Whether or not hospital cases receive more antitoxin than is absolutely necessary, they, at least, cannot be judged by the standard set in private practice where the cases receive treatment promptly.

Our cases show some features which are worth mentioning. The average time for the disappearance of the membrane was two and two-third days and normal temperature averaged three and three-fourth days. Paralysis of the soft palate occurred in only 5 per cent. Other paralysis, 4 per cent. Arthralgia was noticed in only 2.6 per cent. and serum rashes in 16 per cent. Concentrated serum was always used. No anaphylactic phenomena were observed in any of our cases. Our mortality for diphtheria as reported up to January 1, 1912, was 3⅓ per cent.; while for scarlet fever it was 6.5 per cent. This is at least an illustration of the principle that large doses of antitoxin need not be feared, and that it neutralizes all the toxin. The converse applies forcibly to insufficient dosage. Promptness in administration is an important guide to the size of the dose.

The Wesbrook[8] classification was used routinely in examinations for the Klebs-Loeffler bacillus. A, C, and D, the granular types, were regarded as positive and when found three successive negative cultures were required before discharge.

A_1, A_2, B, B_2, C, C_2, and E (the barred types except E), were called doubtful, and when found put the patient back for only one culture instead of three. The solid forms were regarded as negligible. This method is a liberal one as it makes a distinction between the virulent and non-virulent types.

No use was made of the Diazo reaction in diphtheria as a differential sign between a purely serum rash and true scarlet or measles. It occurs in 17 per cent. of scarlet fever cases, 12 per cent. of diphtheria, and 75 per cent. of measle cases. In the latter it might be helpful.

Little difficulty was experienced with the persistence of the Klebs-Loeffler bacillus in the throats of convalescing individuals.

[8] Amer. Jour. Public Hygiene, May, 1907.

This happened only two or three times. The early negative findings were undoubtedly influenced by frequent throat irrigations and sometimes nasal, of normal salt solution or bichloride solution (1 to 12,000) or simple applications of the latter (1 to 4000).

L. M. De Witt and others recommend the application and sprays of fresh cultures in broth of the Staphylococcus pyogenes aureus for persistent Klebs-Loeffler bacilli in the throat. This should not be done until convalescence, when the mucous membrane presents a normal healed surface. There is no incompatibility between the Klebs-Loeffler and the staphylococcus, but the latter assists in reinforcing the normal throat flora.

Max Crohn[9] recommends small doses of antitoxin (2000 units) subcutaneously for post-diphtheritic paralysis and reports good results. We have not tried it, and should hesitate to do so except in very favorable cases for fear of serum sickness.

Bingel[10] recommends intraspinal injections of diphtheria antitoxin for late cardiac failure after this disease. The condition is so grave that anything which gives even remote promise should be tried.

Cumberlage, of England, recommended the use of antitoxin by the mouth. The initial dose was 4000 units, followed up if necessary by 2000 units more. He did not observe serum rashes or joint pains following the use of this method, and obtained results within a few hours after administration.

We tried this with a few cases (5 in number) and selected them with reference to mildness rather than severity of type. It was administered in milk and usually well borne. We used only small doses, but seeing very slow response gave more than he recommended. The average disappearance of nasal discharge was five and one-half days and of membrane on the tonsils seven and one-third days, as opposed to the subcutaneous method which was two and two-third days.

With the injection of diphtheria antitoxin intravenously we have had no experience. E. Freedberger and S. Mita[11] claim from their experiments that larger doses may be borne and that there is less chance of an anaphylactic reaction when applied directly to the blood stream and so avoiding a reaction with the body tissues. In very desperate cases it might appeal to us as offering a better chance to more promptly neutralize the toxins.

Acetone was found in our diphtheria patients in only 28.5 per cent., but only one examination was made for each of the cases. F. Reicher,[12] of Hamburg, found it in 65 per cent. of his diphtheria patients during the febrile stage and in 40.2 per cent. of all other anginas and is, therefore, inclined to regard it as of diagnostic significance. I cannot see that it is needed especially as an aid,

[9] Münch. med. Woch. 1912, lix, 84.
[10] Deutsch. Arch. f. klin. Med., 1911.
[11] Deutsch. med. Woch., February, 1912.
[12] Münch. med. Woch., October, 1911.

for either a laboratory or clinical case of diphtheria will have its appropriate treatment. Even in private practice one should not be satisfied with just one negative culture.

Our routine method of staining for the Kelbs-Loeffler bacillus has been done with the standard Loeffler's methylene blue. Very recently we have tried in conjunction with this a stain proposed by Dr. Marie Raskin[13] in a paper read before the Royal Clinical Institute, of St. Petersburg. The solution is composed as follows: 5 c.c. of glacial acetic acid, 95 c.c. of distilled water, 100 c.c. of 95 per cent. alcohol, 4 c.c. of an old and long-standing methylene blue solution, 4 c.c. of Ziehl's carbol fuschin.

The method is to drop the mixture on the prepared slide and then boil over a flame for eight to ten seconds. After five seconds the slide is washed in water, dried, and examined. The polar bodies appear as deep blue, while the rod is a bright red.

Practically, our stains so far show the rods to be a pinkish color, while the granules stand out very well as dark bodies. Other rods and cocci likewise take the pink stain. From our limited experience in its use, it appears to be a good stain and I think that the polar bodies stand out more prominently than with the methylene blue method alone.

Before closing let me mention a few observations concerning measles and rubella. Our average white count for all ages in both was between 7000 and 8000, somewhat higher than we would expect. All had an increased polymorphonuclear count.

The cervical and submaxillary glands were enlarged in practically all of our rubella cases, but in none markedly so. The submental gland was enlarged in a few cases (recent cases show their presence more often), the post-auricular were enlarged more frequently. In rubella the rash was of the maculo-papular type in 81 per cent.; of the erythematous type in 19 per cent.

In measles, acetone and diacetic acid (each) were present in 22 per cent. which is, I believe, lower than usual. Indican occurred in 88 per cent.

In rubella both acetone and diacetic acid were negative in all cases, a fact which may be found to have some diagnostic significance; indican was positive in 50 per cent.

In conclusion I wish to express my appreciation of the efficient work done in the laboratory by Dr. William H. Peters, the bacteriologist, and by Mr. King and Mr. Bader, of the Ohio-Miami Medical School, whose results are incorporated in this article. To Dr. Samuel Zielonka I am indebted for several valuable translations. It would also be unfair to close without grateful recognition of the services of the internes and nurses who, from time to time, have been on duty at the hospital, for without their help this paper would have been impossible.

[13] Deutsch. med. Woch., December, 1911.

STUDIES ON THE MOTOR FUNCTIONS OF THE STOMACH BY THE USE OF THE GASTRIC AND DUODENAL FISTULAS, ESPECIALLY AS REGARDS THE INFLUENCE OF THE BITTER WATERS AND BITTER SALTS, THAT IS, THOSE CONTAINING MAGNESIUM SULPHATE OR SODIUM SULPHATE.

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The object of the experiments described in this article was to study the effect of various substances, especially salts and waters containing either magnesium sulphate ($MgSo_4$) or sodium sulphate (Na_2So_4), the so-called bitter salts and bitter waters, upon the motor functions of the stomach. This was done by means of the low gastric fistula in one dog and the high duodenal fistula in three other dogs, determining in the former the quantity of residual fluid after a certain length of time, and in the latter the time required for all the fluid to pass, using the two methods synchronously for the study of the liquids in question. The dogs used were strong, healthy, and of moderate size, and had been kept fasting from eighteen to thirty hours before each experiment; the fluid to be tested was introduced by means of the ordinary stomach tube and funnel. If, as occurred several times during these experiments, especially after the use of highly concentrated solutions of the salts, the dog developed symptoms of an acute gastric catarrh, vomiting, anorexia, and the presence of considerable mucus occasionally slightly blood-streaked in the gastric contents, that dog was not used again until all signs and symptoms of the catarrh had entirely disappeared. The experiments were always comparative, that is, the solution to be tested was always compared as to its effect with an equal quantity of some other fluid, sometimes ordinary water, at other times some other solution of the same or of another salt, these experiments following each other after an interval of from one-half an hour to an hour or more, but always on the same day as the motor functions of the healthy stomach vary so markedly under different conditions, and are so much affected by surrounding circumstances, the amount of noise, the presence of unusual sights and sounds, psychic state of the animal, etc., that otherwise the results obtained would be of far less value. The liquids were all given at room temperature (18° C.).

In the case of the gastric fistula the stomach was first drained thoroughly by removing the cork which stopped the opening, and then, after its return, 150 c.c. of fluid was administered, and the

residue withdrawn by removal of the cork in ten minutes (unless otherwise noted in our tables) and carefully measured. In the case of the duodenal fistula the cork was withdrawn and the upper duodenum drained, the cork replaced and 150 c.c. of the liquid given, a few drops of methylene blue or methyl-violet solution being used as an indicator (indigo-carmine powder in the case of the oils). The old method of withdrawing from 0.5 to 1 c.c. of fluid every two minutes was discarded as being far too unphysiological, as unquestionably the emptying of the stomach is dependent not only upon the reaction of the fluid in the duodenum, but also upon its quantity, and the withdrawal of the amount demanded by the older method changes markedly the pressure conditions in the duodenum, and results in the conclusion that the stomach empties itself more rapidly than under more physiological conditions. Our method was to withdraw about 1 c.c. of fluid every ten minutes for the first hour or even longer, then, as the change in the color suggested that the experiment was drawing to its close, every five minutes and finally every two minutes.

In a certain number of our experiments, quantitative determinations of the salt used and of the hydrochloric acid were made in the case of the gastric fistula and of the former alone in the case of the duodenal fistula, and then from our knowledge of the amount of the salt (usually sulphate) in the solution used and on the assumption that the acidity of the pure gastric juice of the healthy dog is practically constant (0.5 per cent.), we have attempted to determine the amount of gastric juice and transudate resulting from the use of the fluid in question in the gastric fistula, and the sum of gastric, duodenal, pancreatic, and biliary secretions, and transudate (or exudate) in the duodenal fistula. We have assumed for this that the amount of absorption of salts and water is *nil*, which is probably practically true in the case of the ten-minute experiment with the gastric fistula, but hardly approximately true with the duodenal fistula, as the time for the substances to be in contact with the mucous membrane is much longer, and the chances of absorption correspondingly greater. Nevertheless, we give the figures for what they may be worth, and in this connection we must not forget the poor powers of absorption of the magnesium salts and of sodium sulphate as many investigations have shown. In our quantitative determinations with the duodenal fistula, we have attempted to obtain the average salt content by taking 1 c.c. of the fluid withdrawn at ten-minute intervals, 0.5 c.c. at five-minute, and 0.2 c.c. at two-minute intervals, making our analysis from the mixed fluid so obtained.

In practically all our experiments, we determined the freezing points of the solutions used in order to determine whether we were dealing with iso-, hypo-, or hypertonic fluids. In a number of cases, notably with Hunyadi and Friedrichshall waters, by adding

enough water to make these fluids practically isotonic, we could obtain comparative results as to the influence of these well-known waters as usually administered, and when diluted to isotonicity, while with the various salts employed by us we could compare the effects of hypo-, iso-, and hypertonic solutions of the same salt by using solutions of different strength. It should be mentioned that the freezing point ($\triangle$) of the dog's serum equals —0.6° C. and not —0.56° C., as in the human being.

As to whether more exact data as regards the motor function of the stomach are to be obtained by the use of the gastric or duodenal fistula, each has its value. By the former we get a better idea of the amount of gastric secretion and transudate called forth; by the latter, especially if our more physiological method is employed, truer knowledge as to the exact time required by the solution to entirely leave the stomach.

Before giving the results of our experiments, the exact figures of which will be found in tabulated form at the end of this article, it may be of interest to briefly review some of the important literature as regards the motor functions of the stomach, especially, of course, the results obtained by the use of the *x*-rays in man and in animals, and of the gastric and duodenal fistulas in animals, and to a less extent, by the examination of the feces and by auscultation and palpation. The discovery of a definite anatomical separation between the fundus and the antrum pylori calls attention anew to the fact that the latter's function is distinct, the more thorough mixing of the liquid or semiliquid food (furnished by the fundus) with gastric juice and ejection into the duodenum. The so-called pyloric reflex determines to a great extent the length of time the food remains in the stomach, the stimulant being mechanical, according to Morris and von Mering, chemical according to the Pawlow school, both playing a part, according to Tobler, and this last seems the most probable. According to many observers, the true peristaltic waves arise practically only in the pyloric portion, although, according to Boldyreff, even in the fasting stomach rhythmic contractions appear at intervals of from one and one-half to two hours.

As to the length of time various fluids remain in the stomach, Cohnheim and Best,[1] found that physiological sodium chloride solution leaves the stomach quickest, water remains longer, and a 2 per cent. sodium chloride solution still longer. They found that the temperature of the fluid did not affect the motility, while Roeder[2] found that temperatures above or below 37° C. stimulate the motility.

According to Cohnheim[3] and Cannon[4] there are autonomous

[1] Zeit. f. physiol. Chemie, 1910, lxix, 117.
[2] Med. Klin., 1909, v, 816.
[3] Zeit. f. physiol. Chemie, 1910, lxix, 102.
[4] Amer. Jour. Physiol., 1906. xvii.

motor centres in the stomach, while the effect of psychic influences upon motility has been especially shown by the former. Perhaps our greatest knowledge of the motor functions of the stomach has come from the use of the *x*-rays in this field, inaugurated by Cannon and by Roux and Balthazar in 1897, and since then employed by many investigators in this connection. An interesting review of the work done along these lines is to be found in an article by Hertz,[5] which includes a number of important personal observations. According to Leven and Barret, 200 c.c. of water leaves the stomach, if already empty, in about twenty minutes, figures closely harmonizing with certain of our experiments on the dog with the gastric fistula, and which suggests that the pyloric sphincter does not become strongly contracted until after the ingestion of food. According to Carnot, Chessevant, and Otto, distilled water and anisotonic salt solutions generally remain longer in the stomach than isotonic solutions, probably due to the inhibition of the pyloric relaxation, and, to quote Hertz's discussion of these researches: "Consequently the chyme when it reaches the duodenum is much more nearly isotonic with the tissue fluids than when it reaches the stomach. The change is brought about in part by the secretion of fluid rich in salt in the case of hypotonic solution and distilled water, and by the secretion of ordinary gastric juice in the case of hypertonic solutions. Osmosis and diffusion undoubtedly help in both cases. The change is much less rapid in hypertonic than in hypotonic solutions, but even very concentrated solutions become almost isotonic before their evacuation from the stomach is complete." These conclusions do not agree with our findings, and the question of the effect of the osmotic pressure of a solution upon the gastric motility is still far from settled. It will be remembered in this connection that the absorptive power of the stomach is very slight in the case of most substances, practically *nil* with water. Although, as a rule, diffusion is determined by the osmotic pressure, Roth and Strauss, and Pfeiffer and Sommer have shown that in the case of the stomach unlike the serous cavities, this law does not hold good, for in this viscus the tendency is toward an osmotic pressure lower than that of the blood serum ($\triangle$ = —0.56° C. in human being, —0.6° C. in dogs). According to Strauss this lower level corresponds to a freezing point of from —0.32° C. to —0.48° C. He therefore calls fluids with a freezing point less than —0.48° C. gastrohypertonic, if above this figure gastrohypotonic. According to this investigator the free hydrochloric acid is only secreted when the stomach contents have reached this point; before this the fluid from the stomach wall is neutral or faintly alkaline. According to Roth and Strauss the reason for these phenomena is that the freezing point of the gastric juice equals —0.48° C.; with

[5] Quarterly Jour. Med., 1910, iii, 373.

hypertonic solutions there is a streaming of water from the blood stream, and probably also a migration of more fixed molecules from stomach contents into plasma than in the reverse direction, while even with isotonic liquids this takes place until a degree of tonicity equal to that of the gastric juice is reached. With hypotonic solutions there is a difference of opinion, v. Mering, Moritz, and others holding that the flow of water from gastric contents into the blood stream is very slight, a view certainly borne out by our experiments, although Pfeiffer and Sommer believe that even here the law of osmotic pressure is followed. Rodari thinks these discrepancies can be explained by variations in osmotic pressure of the gastric juice, "but due to the slight permeability of the gastric mucous membrane to water, the water movement due to differences in osmotic pressure between the stomach contents and blood plasma takes place slowly so that another factor plays a part, and an important one, namely, the osmotic pressure of the stomach juice, which as it were, lies between the two and is capable of great variations, although usually hypotonic." According to the experiments of H. Strauss,[6] "a certain law seems to exist so that hypertonic solutions in the stomach are brought by dilution to a condition of lower osmotic pressure and remain longer in the stomach than hypotonic solutions," and this exactly harmonizes with our findings.

It is very difficult to explain all the facts regarding absorption from and transudation into the stomach on purely physical grounds, especially when we remember that most investigators hold that the gastric juice is of constant not varying composition, although, of course, as studied *extra vitam* by the usual methods, it may show wide variations, due to its degree of admixture with mucus, transudate, and ingesta.

As to the special effect of certain purgatives and laxatives, especially the bitter waters and bitter salts, upon the secretory and motor functions of intestines and stomach, much more work naturally has been done upon the intestinal side. Liebig believed that the action of salts was due to endosmosis, and therefore the greater the concentration of the salt the greater its purgative effect. Aubert, on the other hand, suggested that this was due more to chemical than to physical influences, that the quantity, not the concentration of the salt, was the important factor, and that the purgative action was due to the stimulation of the intestinal nerve-endings by the salt absorbed in the blood. Bauer, Moreau, and Brunton, from experiments with isolated intestinal loops, reached conclusions similar to those of Liebig; Hay suggested that the fluid poured out so abundantly was an exudate, not a transudate: while Hamburger combined the various theories, and suggested

[6] Physiol. Mineral-Stoffwechsel, Berlin, 1906.

that the purgative effect of the bitter salts depends on the increase of fluid in the intestinal canal due to gastric, intestinal, and possibly pancreatic secretion, to lessened absorption and increased peristalsis. Bickel[7] has shown that sodium sulphate and Hunyadi water distinctly inhibit the pancreatic secretion, and that the latter produces a diminution of the gastric secretion, especially of the hydrochloric acid; this was shown by him in the blind Pawlow stomach. According to Heinheimer, sodium and magnesium sulphate inhibit the secretion of hydrochloric acid, while Sasaki found that Carlsbad water occupies a middle position between the excitosecretory and the depressosecretory waters, agreeing with the clinical findings of Jaworski that small repeated doses of Carlsbad water increase the gastric secretion, large doses, if continued, inhibit its secretion more and more. Tausoni and Morfiori believe that the purgative action of the bitter waters is due to the great increase of mucus which hinders absorption, while to lessened absorption F. Frankl also ascribes this action, as he found no increase of peristalsis nor a transudation into the intestine after the injection of sodium sulphate into the blood. J. B. MacCallum, however, found both increased peristalsis and increased passage of fluid from intestinal wall into intestine after the intravenous administration of the bitter salts; according to Headland, Mendel, and others, this same effect is produced when the salts are given by mouth by their absorption in the upper intestine and secretion later into the lower intestine together with a large amount of transudate. Hertz[8] from *x*-ray studies reached conclusions similar to those of Aubert and MacCallum, namely, that saline purgatives cause little or no acceleration in the passage of the chyme through the small intestine, but that the colon is markedly affected, and that "some of the purgative salt must have been absorbed from the stomach or small intestine into the blood from which it acted directly upon the neuromuscular mechanism, producing motor and secretory activity in the way described by MacCallum." Ury,[9] in a most exhaustive series of analyses of the salts and ferments of the feces, after the administration of various purgatives to men and to animals, concluded that the bitter salts in large doses act by causing a local irritation of the nerve plexus lying in the intestinal wall, increasing peristalsis, and calling forth a strong transudation of a watery fluid. The marked increase of peristalsis is not explained by the increase of the fluid, but is primary in nature, and coördinate with the transudation. Mucus was absent, or present in very small amount, and there was a moderate increase of the intestinal juice. In small doses as used in practice for laxative purposes, increased peristalsis and transudation were present, but to a lesser

[7] Berl. klin. Woch., 1906, No. II.
[8] Guy's Hospital Reports, 1909, lxiii.
[9] Arch. f. Verdauungskrankh., 1909, xv, 210, and Biochem Zeitschr., 1910, xxiii, 153.

extent, and here comes into play the poor power of absorption of the magnesium salts, and the retention of their water of solution, and isotony of the fluid contents of the small intestines is not reached. As to the effect of other laxatives, Ury found after senna an increase of fluids, hypersecretion of pancreatic juice, a colossal increase of diastase, absence of pepsin and lipase, and an increase in the secretion of the small intestine, as shown by the presence of maltase, invertin and a trace of nuclease, while, on the other hand, Ascher and Spiro found that senna, rhubarb, cascara, and aloes act only through increased peristalsis, and Brieger, in dogs, and Flemming, in rabbits, found no increase in the intestinal secretion and no reddening of the mucosa in isolated loops of intestine. Magnus[10] found that castor oil produced increased peristalsis in both small and large intestines, senna only in the large intestine; thus, as regards peristalsis, the former acts like large doses of magnesium sulphate, the latter like small doses, according to Ury.

The results of our experiments were as follows:

A. With Hunyadi Janos and Friedrichshall Waters. The detailed results of these as of all our other experiments will be found in tabulated form at the end of this article, and we shall here simply call attention to certain points of interest, especially the influence of the tonicity of the fluid, and the results of quantitative studies of the amount of gastric juice secreted, and the extent of the transudation. The freezing point of Hunyadi water is —1.03° C., of Friedrichshall —1.15°, of tap water —0.03° C., and dog serum —0.6° C., that is, each of these waters is strongly hypertonic, while a dilution of each with an equal amount of tap water will give almost isotonic solution (△ of 50 per cent. Hunyadi = —0.51° C., of 50 per cent. Friedrichshall = —0.6° C.).

A consideration of the figures in the tables will show that the motor functions of the stomach tested both by the gastric and the duodenal fistula methods are very strongly inhibited by these hypertonic waters, while if diluted about to isotonicity, the difference between their action and that of tap water as regards gastric motility is very slight. This and in fact all our experiments have shown that it is impossible to explain the absorption and motor phenomena of the stomach on purely physical grounds alone, as otherwise the almost isotonic 50 per cent. Hunyadi and Friedrichshall solutions would leave far more rapidly than the strongly hypotonic tap water; in reality the latter leaves the organ a little sooner.

The question of the amount of gastric juice and transudate called forth by these waters was considered quantitatively. In Friedrichshall water in 10 c.c. the amount of sulphates calculated as barium sulphate ($BaSo_4$) equals 0.2292 gram, in Hunyadi water

[10] Pflüger's Arch., 1908, cxxii, 251.

0.598 gram.; the acidity of the pure gastric juice of the dog is assumed to be 0.5 per cent.

In Experiments 6, 7, and 8 of our series with the gastric fistula the following figures were obtained; the first two were experiments of ten minutes, the last of twenty minutes; 150 c.c. of fluid was given in each case.

EXPERIMENT 6.

Solution used.	Amount of fluid obtained.	Acidity in $\frac{n}{10}$ NaOH.	Sulphates in 10 c.c. as $BaSO_4$.	Gastric juice.	Transudate.
Tap water	46 c.c.	6	0.0	2.0 c.c.	
50 per cent. Hunyadi	77 c.c.	4	0.2388 gram	2.5 c.c.	13.0 c.c.
Hunyadi	104 c.c.	4	0.4948 gram	3.7 c.c.	15.3 c.c.

EXPERIMENT 7.

Tap water	79 c.c.	6	0.0	3.5 c.c.	
50% Friedrichshall	76 c.c.	6	0.0972 gram	3.3 c.c.	8.3 c.c.
Friedrichshall	121 c.c.	4	0.1928 gram	3.3 c.c.	16.6 c.c.

EXPERIMENT 8.

Tap water	18 c.c.	60	0.0	7.9 c.c.	
50% Friedrichshall	30 c.c.	55	0.0546 gram	12.0 c.c.	2.7 c.c.
Friedrichshall	74 c.c.	23	0.1289 gram	12.4 c.c.	19.1 c.c.

These experiments show, in the first place, that in ten minutes very little gastric juice is secreted, while in twenty minutes the percentage is much higher. In the second place, a considerable transudation is present with both solutions, more with the hypertonic than with the isotonic fluids, but transudate and gastric juice combined were not enough to account for the amount of liquid remaining in the stomach in the case of the pure Hunyadi and Friedrichshall waters, and, therefore, these waters besides calling forth considerable transudation and some secretion of gastric juice, undoubtedly also strongly inhibit the motor functions of the stomach. Number 4 of our series of experiments with the gastric fistula was very instructive in that it showed that this inhibitory effect disappears quickly after the hypertonic solution has left the stomach; with oil, however, which does not leave the stomach completely, but coats the mucous membrane with a covering difficult to remove, this inhibiting influence persists much longer, as seen in Experiment 5.

It must not be forgotten, however, that all these results are based on the assumption that during the short time of the experiment practically no absorption of salts or water by the stomach takes place. Occasionally in the case of these waters and also with strongly hypertonic solutions of Carlsbad salts and magnesium sulphate, in some instances a true, acute gastric catarrh, with all the characteristic signs and symptoms, was produced, necessitating the discontinuance of the experiments until the stomach was completely cured.

In the case of the duodenal fistula, in Experiment 6, a quantitative sulphate determination was made with the following results:

Solution used (150 c.c.).	Time to pass duodenal fistula.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates in 10 c.c. as $BaSO_4$.
Hunyadi	2 hours 10 minutes	8	0.1374 gram
50% Hunyadi	1 hour 25 minutes	7	0.112 gram

This would mean, assuming that there has been practically no absorption of salts or water, that after the giving of 150 c.c. pure Hunyadi water, the sum of the biliary, gastric, duodenal, pancreatic, and mucous secretions and of transudate called forth equalled 503 c.c., while after 150 c.c. of almost isotonic 50 per cent. Hunyadi, only 250 c.c. was called forth. Another experiment in this connection may be of interest: To one of the duodenal fistula dogs was given 130 c.c. pure Hunyadi water and all the fluid from the duodenal fistula collected. Although, of course, the major portion must have passed by the fistulous opening along the much broader upper intestine, nevertheless, in one and one-half hours 182 c.c. was obtained from the fistula.

B. With Carlsbad Salts. We made a few experiments with natural and artificial Carlsbad salts (the latter, as a rule, being 44 parts Na_2SO_4, 36 parts $NaHCO_4$, 18 parts NaCl, and 2 parts K_2SO_4). Of the waters obtained at the springs, Sprudel has a freezing point of —0.307° C., Muhlbrunnen —0.293° C., Franz Joseph —0.290° C.; of solutions of the natural salts, in 1 per cent. solutions Δ = —0.47° C., in 5 per cent. Δ = —1.88° C., while of the artificial salts in 2 per cent. solution Δ = —0.3° C., in 5 per cent. Δ = —0.77° C., that is, of the artificial salts a 3 per cent. solution is about isotonic, a 10 per cent. solution strongly hypertonic. A considerable inhibition of gastric motility is seen with hypertonic solutions with both methods, while, as with Hunyadi and Friedrichshall water, even with isotonic solutions some transudation is called forth, and the solutions take a slightly—although only very slightly—longer time to entirely leave the stomach than ordinary tap water. The secretion of gastric juice after Carlsbad solutions is certainly no more, and probably slightly less than after ordinary water.

One quantitative experiment (Number 3) was made with the gastric fistula as follows:

Experiment 1.

Solution used (150 c.c.).	Amount obtained in ten minutes.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates in 10 c.c. as $BaSO_4$.	Amount of gastric juice.	Amount of transudate.
Tap water . .	12 c.c.	60	0.0	5.2 c.c.	
3% solution of artificial salt .	22 c.c.	20	0.2605 gram	3.2 c.c.	8.5 c.c.
10% solution of artificial salt .	88 c.c.	10	0.7277 gram	6.4 c.c.	47.2 c.c.

This experiment again calls attention to the enormous amount of transudate called forth by strongly hypertonic solutions, and also to their marked inhibitory effects upon gastric motility. These strong solutions of Carlsbad salt frequently showed their markedly irritating effect upon the mucous membrane by producing the typical symptoms of an acute gastritis, the secretion of mucus in large amount, sometimes blood-stained, anorexia, vomiting, etc.

C. With Magnesium Sulphate (Epsom Salt—$MgSo_4$). Of solutions of magnesium sulphate in solutions of 1 per cent. $\triangle$ = —0.13° C., of 3 per cent. $\triangle$ = —0.32° C., of 10 per cent. $\triangle$ = —0.71° C., and 20 per cent. $\triangle$ = —1.45° C., and a 7.5 per cent. solution is practically isotonic. These figures were obtained with solutions of the ordinary Epsom salt bought at the drug store. In 10 c.c. of a 20 per cent. solution, the amount of sulphates calculated as $BaSo_4$ = 1.8937 grams.

With the weak solutions of this salt we had a good opportunity to study the effect of strongly hypotonic solutions. With the duodenal fistula, the 1 per cent. solution and water seemed to take practically the same time, the 3 per cent. solution distinctly longer —an interesting fact when we remember that the latter contains more of the salt in solution and is closer to isotonicity.

Two quantitative experiments with the gastric fistula (Numbers 2 and 3) were made with the following results:

Experiment 2.

Solution used (150 c.c.).	Amount obtained in ten minutes.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates of 10 c.c. as $BaSO_4$.	Amount in gastric juice.	Amount of transudate.
Water . . .	24 c.c.	8	...	1.4 c.c.	
1% $MgSO_4$ . .	36 c.c.	30	...	7.9 c.c.	
3% $MgSO_4$ . .	58 c.c.	12	...	5.1 c.c.	

Experiment 3.

Water . . .	29 c.c.	13	0.0	2.5 c.c.	
7.5% $MgSO_4$.	38 c.c.	12	0.4512 gram	3.3 c.c.	10.6 c.c.
20% $MgSO_4$.	98 c.c.	8	1.2296 gram	6.0 c.c.	28.5 c.c.

These figures again show the marked inhibition of gastric motility and the stimulating effect upon transudation of strongly hypertonic solutions; and also that the difference between the effects of water, isotonic and hypotonic solutions upon gastric motility is but slight—the salt solutions retarding it a little, possibly due to the transudate they undoubtedly call forth, while as regards the amount of gastric juice secreted, some solutions seem to call forth more than water, others less.

D. With Sodium Sulphate (Glauber's Salt—Na_2SO_4). The 1 per cent. solution of this salt has a freezing point of —0.36° C., the 3 per cent. solution of —0.82° C. The results obtained harmonized with those previously described as regards the influence of hypertonic and hypotonic solutions.

E. With Olive and Castor Oils. These experiments simply called attention to the already well known fact that oils markedly inhibit the motor functions of the stomach; of the two castor oil retarded the gastric movements most, and this was probably due to its greater irritating effect, as, with this as with the other substances tested, the stomach seems to act in a manner just opposite to the intestine, that is, the more the mucous membrane of the former viscus is irritated, the more its motor function is inhibited.

F. With Other Substances. We have added a few experiments made with various other substances which may be of some interest. Strong tea seemed to inhibit the gastric motility, and also mesothorium emanations, although to a less extent.

Two experiments were made with the gastric fistula with the well-known Roumanian diuretic water, Caciuglata, of which the freezing point is —0.17° C.; that is, it is strongly hypotonic. It and tap water left the stomach in practically the same time, and in this, as in many other cases, we have repeated the experiment in the reverse direction, that is, if we gave water first and then the fluid to be tested in the first experiment, this order was reversed in the second; by this means our results should be more accurate, for if the animal is more fatigued at the time of administration of the second dose, and thereby perhaps the motor function slightly inhibited, this will be discounted by the results obtained in the reversed experiment. With this water we performed two quantitative experiments, here comparing the phosphate-content (as magnesium phosphate) of the fluid obtained from the gastric fistula with that of the diuretic water itself, in 25 c.c. of which there is 0.0063 gram. The results of these experiments were as follows:

Solution used (150 c.c.).	Amount obtained in fifteen minutes.	Acidity in $\frac{N}{10}$ NaOH.	Phosphates in 25 c.c. as Mg- phosphate.	Amount of gastric juice.	Amount of transudate.
Water . . .	59 c.c.	29	0.0	12.5 c.c.	
Caciuglata water	44 c.c.	37	0.00325 gram	11.8 c.c.	9.6 c.c.
Caciuglata water	22 c.c.	30	...	4.8 c.c.	
Water . . .	18 c.c.	25	...	3.3 c.c.	

In a number of other experiments both with the gastric and the duodenal fistula, we could show the extremely marked inhibitory effect of various emotions, such as fatigue and of surrounding disturbances, such as noise, upon the motor function of the stomach. This, of course, accentuates the fact that an animal should never be used for experimental purposes until it has become habituated to standing for a considerable period of time without being fatigued, and also that it is essential that the experiments be carried out in a room as free as possible from noise, excitement, and unusual sights and sounds.

The main conclusions which we may draw from this series of experiments are as follows:

By the use of both the gastric and the duodenal fistula, and in the latter case we suggest our modification of the usual method as a much closer approximation of physiological conditions, we may obtain data of comparative exactness as to the influence of various substances upon the motor functions of the stomach. By the duodenal method we obtain figures of greater exactness as to the comparative times required by various liquids to entirely leave the stomach, by the gastric method we learn more about the effect of these liquids upon gastric secretion and transudation; we would suggest that the two methods always be employed simultaneously.

As to the influence of the various bitter waters and solutions of the bitter salts—all of which depend in the main for their action upon magnesium or sodium sulphate, strongly hypertonic solutions or waters markedly inhibit gastric motility, besides producing a great transudation into the stomach as well as a secretion of gastric juice, which latter may be more or less than that obtained after the administration of ordinary tap water. If these salts are given in very strong solution, their irritating effects are seen in certain instances by the appearance of the typical signs and symptoms of an acute gastritis.

By the use of quantitative analyses of the hydrochloric acid and sulphates in the fluid obtained from gastric or duodenal fistula, we may get some idea of the extent of the secretion and transudation.

Isotonic solutions leave the stomach much sooner than strongly hypertonic solutions, and do not call forth so much transudate as the latter, and much less frequently, although occasionally, produce irritating effects upon the gastric mucous membrane. This suggests the inadvisability of using hypertonic solutions of the bitter salts in gastric disorders with atony or with a diseased condition of the mucous membrane, even if thereby the desired laxative or purgative effect is diminished.

As a rule isotonic and hypotonic solutions leave the stomach a little less rapidly than the very hypotonic tap-water, possibly due to the transudate called forth by the former fluids, although this is of much less extent than after hypertonic solutions; the secretion of gastric juice may be slightly more or slightly less with these solutions than with ordinary water. This again calls attention to the fact that it is impossible to explain the motor and absorptive phenomena of the stomach on purely physical grounds, even when, in addition to the ordinary laws governing diffusion and osmosis, we assume the interposition between gastric cavity and gastric wall of a gastric juice of varying tonicity.

A comparison between the action of the bitter salts and bitter waters upon the motor functions of the stomach with those of the intestine, shows that their action is reversed, inhibitory in the former case, stimulating in the latter, while in both cases transudation is markedly stimulated.

The complete figures of all the experiments follow:

Motility Experiments.

A. With Hunyadi Janos (H) and Friedrichshall (F) Waters.

First Series, with Gastric Fistula.

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	22 c.c.
	H	150 c.c.	10 minutes	91 c.c.
	F	150 c.c.	10 minutes	71 c.c.
2	Water	150 c.c.	10 minutes	68 c.c.
	F	150 c.c.	10 minutes	122 c.c.
	H	150 c.c.	10 minutes	98 c.c.
3	Water	150 c.c.	10 minutes	44 c.c.
	H	150 c.c.	10 minutes	104 c.c.
4	Water	150 c.c.	10 minutes	28 c.c.
	Water with mesothorium	150 c.c.	10 minutes	38 c.c.
	F	150 c.c.	10 minutes	92 c.c.
	Water	150 c.c.	10 minutes	48 c.c.
	H	150 c.c.	10 minutes	107 c.c.
5	Water	100 c.c.	10 minutes	24 c.c.
	Olive oil	100 c.c.	10 minutes	84 c.c.
	H	100 c.c.	10 minutes	85 c.c.
	F	100 c.c.	10 minutes	104 c.c.
6	Water	150 c.c.	10 minutes	46 c.c.
	50 per cent. H	150 c.c.	10 minutes	77 c.c.
	H	150 c.c.	10 minutes	104 c.c.
7	Water	150 c.c.	10 minutes	79 c.c.
	50 per cent. F	150 c.c.	10 minutes	76 c.c.
	F	150 c.c.	10 minutes	121 c.c.
8	Water	150 c.c.	20 minutes	18 c.c.
	50 per cent. F	150 c.c.	20 minutes	30 c.c.
	F	150 c.c.	10 minutes	74 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	H	150 c.c.	1 hour 36 minutes
	F	150 c.c.	1 hour 17 minutes
2	Water	150 c.c.	1 hour 18 minutes
	H	150 c.c.	2 hours 9 minutes
3	F	150 c.c.	2 hours 25 minutes
	Water	150 c.c.	1 hour 52 minutes
4	50 per cent. F	150 c.c.	1 hour 17 minutes
	F	150 c.c.	2 hours 19 minutes
5	H	150 c.c.	2 hours 10 minutes
	50 per cent. H	150 c.c.	1 hour 25 minutes

B. WITH CARLSBAD SALT, NATURAL (N) AND ARTIFICIAL (A).

First Series, with Gastric Fistula.

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	1 per cent. N	150 c.c.	10 minutes	68 c.c.
	5 per cent. N	150 c.c.	10 minutes	92 c.c.
	1 per cent. N	150 c.c.	20 minutes	3 c.c.
2	Water	150 c.c.	20 minutes	4 c.c.
	1 per cent. N	150 c.c.	20 minutes	8 c.c.
3	Water	150 c.c.	10 minutes	12 c.c.
	3 per cent. A	150 c.c.	10 minutes	22 c.c.
	10 per cent. A	150 c.c.	10 minutes	88 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	Water	150 c.c.	55 minutes
	5 per cent. N	150 c.c.	1 hour 42 minutes
2	1 per cent. N	150 c.c.	1 hour 4 minutes
	5 per cent. N	150 c.c.	1 hour 28 minutes

C. WITH EPSOM SALT.

First Series, with Gastric Fistula.

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	3 per cent. E	150 c.c.	10 minutes	54 c.c.
	1 per cent. E	150 c.c.	10 minutes	66 c.c.
	Water	150 c.c.	10 minutes	69 c.c.
2	Water	150 c.c.	10 minutes	24 c.c.
	1 per cent. E	150 c.c.	10 minutes	36 c.c.
	3 per cent. E	150 c.c.	10 minutes	58 c.c.
3	Water	150 c.c.	10 minutes	29 c.c.
	7½ per cent. E	150 c.c.	10 minutes	38 c.c.
	20 per cent. E	150 c.c.	10 minutes	98 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	1 per cent. E	150 c.c.	1 hour 1 minute
	3 per cent. E	150 c.c.	1 hour 42 minutes
2	3 per cent. E	150 c.c.	1 hour 58 minutes
	1 per cent. E	150 c.c.	1 hour 37 minutes
3	Water	150 c.c.	1 hour 34 minutes
	1 per cent. E	150 c.c.	1 hour 26 minutes

D. WITH GLAUBER'S SALT (G).

First Series, with Gastric Fistula.

Experment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	41 c.c.
	1 per cent. G	150 c.c.	10 minutes	84 c.c.
	3 per cent. G	150 c.c.	10 minutes	98 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	1 per cent. G	150 c.c.	1 hour 21 minutes
	3 per cent. G	150 c.c.	1 hour 35 minutes

E. WITH OLIVE OIL AND CASTOR OIL.

First Series, with Gastric Fistula.

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Olive oil, 30 c.c. Water, 120 c.c.	150 c.c.	10 minutes	106 c.c.
	Castor oil, 30 c.c. Water, 120 c.c.	150 c.c.	10 minutes	82 c.c.
2	Water	100 c.c.	10 minutes	24 c.c.
	Olive oil	100 c.c.	10 minutes	84 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	Olive oil, 30 c.c. Water, 120 c.c.	150 c.c.	1 hour 38 minutes
	Castor oil, 30 c.c. Water, 120 c.c.	150 c.c.	2 hours 24 minutes
2	Olive oil	40 c.c.	2 hours 43 minutes
	Castor oil	40 c.c.	3 hours 40 minutes

F. DIVERSE OBSERVATIONS.

First Series, with Gastric Fistula.

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	54 c.c.
	Water c., 0.1 gram phenolphthalein	150 c.c.	10 minutes	76 c.c.
2	Water	150 c.c.	10 minutes	54 c.c.
	Strong tea	150 c.c.	10 minutes	80 c.c.
3	Water	150 c.c.	10 minutes	28 c.c.
	Water c., mesothorium (14,000 Mache-units)	150 c.c.	10 minutes	38 c.c.
4	Water	150 c.c.	15 minutes	59 c.c.
	Caciuglata water	150 c.c.	15 minutes	44 c.c.
5	Caciuglata water	150 c.c.	15 minutes	30 c.c.
	Water	150 c.c.	15 minutes	25 c.c.

Second Series, with Duodenal Fistula.

Experiment.	Substance.	Amount.	Time.
1	Water, 145 c.c. Alcohol, 5 c.c.	150 c.c.	1 hour 34 minutes
	Water, 145 c.c. Alcohol, 5 c.c. Phenolphthalein, 0.1 gram	150 c.c.	1 hour 57 minutes
2	Water	150 c.c.	1 hour 34 minutes
	Strong tea	150 c.c.	2 hours 10 minutes
3	Water	150 c.c.	55 minutes
	Water c. mesothorium (8400 Mache-units)	150 c.c.	1 hour 36 minutes
4	Water	150 c.c.	1 hour 28 minutes
	Water c. mesothorium (14,000 Mache-units)	150 c.c.	2 hours 21 minutes
5	Fachingen water	150 c.c.	1 hour 28 minutes
	Selters water	150 c.c.	1 hour 4 minutes

THE MORE COMMON FORMS OF CARDIAC IRREGULARITY, WITH THE REPORT OF A CASE OF HEART-BLOCK.[1]

By Thomas A. Claytor, M.D.,

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This subject has been taken up because I believe that it has been too much neglected by the rank and file of internists. I think that one might say without fear of contradiction that without some previous knowledge gained by the instrumental study of the pulse, either with the polygraph or the electrocardiagraph, there are but few who are able to interpret, with any degree of accuracy, the various forms of irregular pulse and are, therefore, unable to give them their proper value as to prognosis and treatment.

That such knowledge may be at times of great importance I hope to show in the following pages.

In the last sixteen years, epoch-making discoveries have materially advanced our knowledge of the histological anatomy of the heart and of its rhythmic action. In fact, A. R. Cushny[2] said that although the study of the pulse had extended as far back as

[1] Read before the American Climatological Association, June 11, 1912.

[2] Amer. Jour. Med. Sci., 1911, p. 1198.

medical history, more progress had been made, in certain directions, in the last fifteen years than in the previous century. As pioneers in the work upon cardiac arrhythmia, the names of Mackenzie, Wenckebach, and Hering probably stand out most prominently.

Putting aside any discussion as to the relative merits of the neurogenic or the myogenic origin of the heart beat, it is found most convenient to study cardiac arrhythmia, keeping always before us the qualities which have been assigned to the heart muscle, which are: (1) Stimulus production, the power to produce a stimulus which will excite the heart to contract; (2) excitability, the power to receive a stimulus; (3) conductivity, the power to convey a stimulus from one part of the heart to another; (4) contractility, the power to contract on being stimulated; (5) tonicity, the power to remain in a certain degree of contraction even when the active stimulation has ceased.

Under normal conditions the cardiac contraction begins in the specialized tissue at the junction of the descending cava and the right auricle, spreading thence to the rest of the heart. This, the sino-auricular node (Keith and Flack[3]), is then the pace-maker of the heart and the rhythmic contraction having its origin here is called the fundamental rhythm. In the wall of the right auricle near the coronary sinus is another specialized area, the auriculoventricular node (Tawara[4]), and it is from this point that arises the auriculoventricular bundle of Kent[5] and His, Jr.,[6] which forms the connecting link for impulses between the auricles and ventricles dividing into two limbs, the one passing to the right and the other to the left ventricle.

While there are instances of cardiac irregularity which are difficult to classify, the majority fall under the following heads: (1) Sinus or youthful arrhythmia; (2) premature contraction or extra systole; (3) heart-block (partial or complete); (4) the wholly irregular pulse (auricular fibrillation); with perhaps the addition of (5) the pulsus alternans, though the last named is an irregularity as to volume rather than as to time.

Some authors assign each of these forms of irregularity to a disorder of some one of the special qualities of the cardiac muscle. Thus sinus arrhythmia is said to be due to disturbance of the sino-auricular node in its impulse producing quality, the extra systole to disturbance of irregularity of the muscle; heart-block to disturbance of conductivity; auricular fibrillation to disturbance of contractility. If this be true, the whole study of cardiac arrhythmia is greatly simplified, but it has not yet been proved.

[3] Jour. Anat. and Physiol., 1907, xli, 172.

[4] Das Reizleitungssystem des Säugatierherzens, Jena, 1908.

[5] Jour. of Physiol., 1893, xiv, 233 to 254.

[6] Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen, Arbeiten aus der Medizinschen Klinik, Leipzig, 1893, p. 14 to 49

I shall now briefly consider the most striking characteristics of the above named forms of arrhythmia as they are portrayed in polygraphic tracings, together with their etiology, pathology, diagnostic, and prognostic value.

As the appreciation of the abnormal polygraphic tracing is absolutely dependent upon an understanding of the normal, we may with profit refresh our memories by a brief consideration of Fig. 1. It may be seen that in the venous tracing there are three distinct upward (positive) waves (*a*, *c*, and *v*) and as many downward (negative) waves (*x*, *x'*, and *y*). The *a* wave in the venous tracing is produced by the state of increased pressure in the jugular vein resulting from the contraction of the right auricle; the *c* wave, while it is not wholly due to the carotid pulsation, for all clinical purposes may be considered to make its appearance synchronously with the beat of that vessel at the same level of the neck. The time between *a* and *c* is known as the *a–c* interval, and is of great importance, as it determines the state of conductivity between the

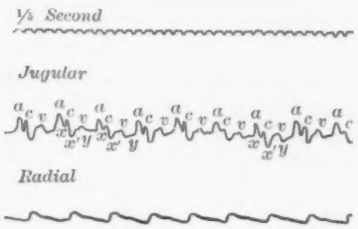

FIG. 1.—Polygraphic tracing of the normal.[7]

auricles and ventricles. The *v* wave, often called the ventricular wave, makes its appearance during ventricular systole, reaching its highest point just before the auriculoventricular valves open. The negative waves *x* and *x'* (usually considered as one), are probably the result of three factors: the relaxation of the auricular walls in early diastole; the state of negative intrathoracic pressure consequent upon the ventricular systole; and the dragging down of the auriculoventricular septum during ventricular contraction. The *y* wave occurs as the result of a state of negative pressure in the ventricles during their diastole, at the same time the auriculoventricular valves open and allow the blood to pass into the ventricles.

The arterial tracing (usually the radial) is necessary for the identification of the important elements of the venous curve.

[7] Through a misunderstanding the identification markings were not reproduced in the figures, but as the writing pens were of equal length the fixation points may be taken from the right border of the tracings.

Thus the *c* wave may be determined by the fact that it appears one-tenth of a second before the radial impulse, the *a* wave because it appears one-fifth of a second before the *c* wave, and the *v* wave by the fact that its apex occupies the same relative position in the venous tracing as does the dicrotic notch in the radial. As pointed out by Lewis,[8] the proper identification of the *v* wave may be of considerable importance in the correct reading of a tracing in which heart-block is suspected.

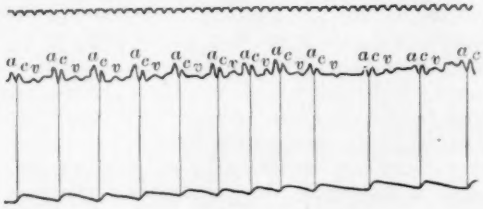

FIG. 2.—Sinus or youthful arrhythmia.

SINUS, OR YOUTHFUL ARRHYTHMIA, may best be described as a difference in the time rate of the cardiac contractions with but little difference, if any, in their force. When venous and arterial tracings are taken simultaneously it will be noted that they are perfectly synchronous in their corresponding details. The arterial tracing will show the systolic peaks to be of about the same height but at varying distances from each other. The irregularity is best seen in a slow pulse, since rapidity, by reducing the diastolic pause, has a tendency to lessen the abnormality. A similar form of arrhythmia may be produced in normal individuals by causing them to take some forced inspiration. The pulse will be found to become more rapid during inspiration and slower during expiration. The cause of sinus irregularity is reflex, coming through the vagi, and does not have its origin in the heart itself. It is observed in young and nervous individuals, also during convalescence from illnesses such as epidemic influenza, etc. It may or may not be noted by the patient, often it is not, though occasionally the diastolic pause is so prolonged as to produce cerebral anemia with syncope. The prognosis is good in all cases. It may be relieved by atropia.

EXTRASYSTOLE. According to Mackenzie,[9] the term "extrasystole" should be limited to those premature contractions of auricle or ventricle in response to a stimulus from some abnormal point of the heart, but where otherwise the fundamental or sinus rhythm of the heart is maintained.

[8] British Med. Jour., 1911, i, 593.
[9] Diseases of the Heart, 1908, p. 142.

Clinically there are recognized three varieties of extrasystole: the auricular, the ventricular, and the auriculoventricular, depending upon the point from which the abnormal stimulus takes its origin. Before going further it may be well to call attention to some physiological facts. It has been shown that if the ventricle be stimulated at any time during diastole (the receptive period of the cycle) it will respond by contracting, but that the force of the contraction is entirely independent of the strength of the stimulation. In other words, the ventricle responds with its entire strength to any stimulus which is sufficient to cause a contraction; the "all or nothing" phenomenon of Bowditch. During systole the ventricle is in the so-called refractory period of the cycle, when it will fail to respond to any stimulation. The strength of the ventricular contraction depends on the amount of energy which there has been time to accumulate. If then the stimulation has been premature the contraction will be feeble, if delayed, correspondingly strong.

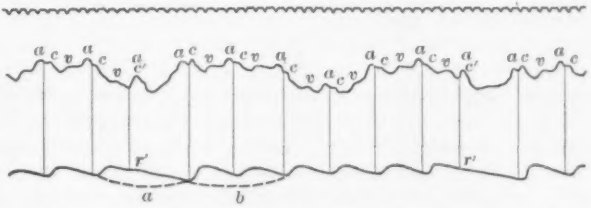

FIG. 3.—Showing extraventricular systoles, r' and r', the one toward the right being too weak to appear in the radial tracing.

In Fig. 3 we have an example of ventricular extrasystole. In the radial tracing at r' may be seen the evidence of a premature and weak pulse beat. In the venous tracing the peak marked c' represents the premature ventricular contraction. It corresponds in general outline fairly well with the c peaks, but is earlier in the cycle and is quite a little higher; in this instance the ventricular contraction has occurred at the same time as the auricular, thereby throwing the a wave and the c wave together, which accounts for its unusual height. This auricular contraction is not followed by the usual ventricular contraction because the ventricle was in systole (the refractory stage) at the time the auricular impulse reached it. This accounts for the longer pause after r', which is known as the compensatory pause. If a measurement be made it will be found that the space between the radial pulsation immediately preceding r', plus that immediately following it, is the same as the distance occupied by two whole cycles of the regular beating ventricles. In other words ($a = b$). It may also be determined by measurement that the auricular rhythm is not disturbed,

that is, the *a* waves occur at practically regular intervals from each other in spite of the disturbed ventricular rhythm as shown by the extrasystole. In some instances the *c* wave actually precedes the *a* wave in the venous tracing. Occasionally in a slowly beating heart the ventricle has had time to recover sufficiently after an extrasystole to respond to the auricular impulse as it would if there had been no extraventricular beat, and we have then an interpolated ventricular contraction. The impulse for a ventricular extrasystole has its origin in that portion of the bundle of His beyond the node of Tawara or in its ramifications in the ventricle.

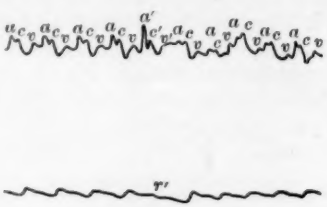

FIG. 4.—Auricular extrasystole.

FIG. 4 is an example of an auricular extrasystole. The radial tracing shows the abortive ventricular beat, the venous tracing presents an unusually early *a* wave, which is followed by the premature *c* wave. At times the *a* wave may come so early as to coincide with the *v* wave of the preceding cycle, at which times it is often unusually high. The impulse for the auricular extrasystole has its origin in some other portion of the specialized auricular tissue than the sinus.

The auriculoventricular extrasystole takes its origin from the node of Tawara. In this form the auricle and ventricle contract simultaneously. It is a more difficult form to identify from the polygraphic tracings than the other two.

So far the exact value, from a clinical point of view, of the differentiation of the three varieties of extrasystole, has not been definitely determined, but it seems very likely that with a more complete understanding of the subject this will be developed.

THE PATHOLOGY OF EXTRASYSTOLE. Extrasystole evidently occurs because of an increased irritability of the specialized cardiac tissue (primitive tube of Mackenzie) so that impulses are received from other points than the sino-auricular node. The pathological lesions when present are of the sclerotic type, hence the condition is most often seen in those who suffer from arteriosclerosis or where there are fibroid changes in the heart from other causes, such as rheumatism. It may be seen at any age, though it is, of course, more common in those past middle life. There seems to be a growing tendency to consider extrasystole an evidence of serious

change in the heart muscle, in spite of the fact that experience has taught us that in many instances it may be present for long periods without other signs of heart disability. Gastro-intestinal disturbances are not infrequently the cause of extrasystole, as is also the excessive use of tobacco.

There may or may not be subjective symptoms of this disorder. Some patients are entirely oblivious to the abnormality, while others are greatly annoyed by a fluttering sensation in the region of the heart or they complain of the violent throb which follows the long pause; some have a sensation of great weakness when the heart is intermitting. Some in fact become so disturbed and nervous that they are almost typical neurasthenics. Medication directed toward the correction of this disorder is very unsatisfactory. The underlying cause must be saught.

Heart-block (Partial or Complete). This form of irregularity is much less common than those just described, and is due to a disturbance of conductivity. The impulse which starts at the sino-auricular node may be delayed or entirely obstructed in its progress to the rest of the heart, resulting in partial or complete heart-block. The interruption may take place at the sino-auricular or at the auriculoventricular junction, and, according to some, at the interventricular junction (dissociation of the ventricles). The most usual and most important of these is the auriculoventricular heart-block which may be either functional or organic. Functional block, as a rule, results from excessive doses of drugs of the digitalis group. This accident, however, is much more likely to happen in cases where the bundle of His is diseased. Organic block is due to disease of the bundle of His or the tissue immediately surrounding it. The common causes then are sclerotic changes in the coronaries with the usual results or old rheumatic inflammation. Rarely, however, the bundle of His may itself be the seat of a growth such as gumma, or may be pressed upon by such a tumor. The first indication of heart-block is a lengthening of the *a–c* interval (the time between the appearance of the *a* wave and the *c* wave in the venous tracing, see Fig. 6). In other words, the ventricular contraction does not follow the auricular as soon as it should. This lenghthening of the *a–c* interval may be for a long time the only evidence of interference in conduction, then the impulse may from time to time fail to get through, resulting in the dropping of a ventricular beat. This may occur at regular or at irregular intervals, and if the block becomes complete, the ventricle assumes its own rhythm which is much slower than that of the auricle. It is in these cases that the Stokes-Adams syndrome is observed.

In organic heart-block the prognosis is necessarily grave, though there are cases on record which have lived for a number of years after the development of the condition. Of course, the cardiac

capacity is reduced in proportion to the degree of block. The functional cases usually recover promptly on the removal of the cause. In those rare instances where the symptoms result from the effects of a gumma upon the bundle of His, antiluetic treatment may be resorted to with some hope of success. It is easy to see that the use of digitalis in cases of heart-block might be fraught with great danger because of its tendency to delay transmission of the impulse from the auricles to the ventricules. James Mackenzie,[9] however, makes the following statement: "The presence of heart-block is not necessarily a contraindication to the use of digitalis. When it is complete it cannot interfere with the conduction of the *a–v* bundle, for conduction is abolished, and so far there is no evidence that digitalis has any effect on the idioventricular rate." Drugs of this group would certainly appear to be contraindicated where there is a tendency to heart-block, and, if used at all, it should be with the greatest caution.

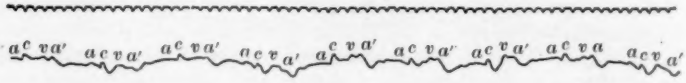

FIG. 5.—Polygraphic tracing from a case of 2 to 1 heart-block. Radial pulse about 37 to the minute. The *a′* waves are auricular contractions which were not followed by ventricular contractions.[10]

Fig. 5 is from a case of heart-block of the 2 to 1 type, the history of which is briefly as follows:

H. B., white male, aged forty-seven years, married, a manufacturer. His parents had been long-lived, and his own health, when a young man, had been excellent. When aged twenty-seven years, he became infected with lues, which was not treated for six months. He then became quite ill and the real condition was recognized, when he received proper medication for a few months continuously, and for years, off and on, for the disease continued to manifest itself from time to time. At thirty-five he had typhoid fever severely. He then enjoyed good health until he was forty-one, when he had several fainting attacks. There was no special discomfort, simply temporary loss of consciousness. At this time a heart murmur was discovered, but there were no symptoms

[9] Heart, 1911, No. 4, p. 293.

[10] In other portions of Tracing No. 5 where the radial dicrotic notch came out clearly it could be satisfactorily demonstrated that the *a* waves were no part of the *v* waves.

of cardiac insufficiency, unless the attacks of syncope were to be attributed to this cause. When aged forty-five years he had an attack of either la grippe or rheumatism (it was difficult from his description to say which), but during the illness heart symptoms developed, and three months later swelling of the feet and dyspnea. During this attack he had peculiar fainting spells. There would be what he described as a rushing sensation from the heart to the head and then unconsciousness lasting from one to five seconds. There was usually time for him to reach the bed or a chair before he would faint, but not always. The heart seemed to stop at the time of the seizure. At times vomiting of blood with great weakness followed. On examination the heart was found to be slightly enlarged, a systolic murmur was heard all over the precordia, with maximum intensity at the apex and transmitted to the axilla. There was also a diastolic murmur heard all over the precordia, the second aortic was faint, and the second pulmonary accentuated. The diastolic murmur was not a typical aortic insufficiency murmur or did the radial tracing conform to the type of that lesion.

Unfortunately I was only able to observe this interesting case for a few days, as he was a transient. A Wassermann reaction was negative, and as there is some doubt as to the advisability of the use of salvarsan in those suffering from severe heart lesions, I hesitated to administer that preparation, but I advised a course of mercurial injections, and my patient went to his home with the avowed intention of returning for treatment, but as yet I have heard nothing from him.

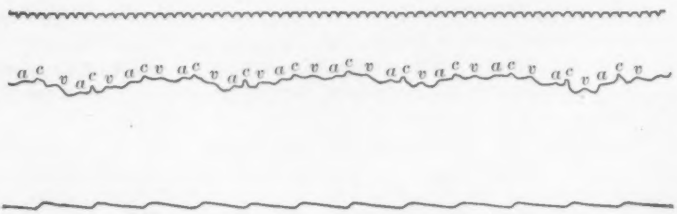

FIG. 6.—Polygraphic tracing taken between attacks, from the case of heart-block here reported. Delay in the *a-c* interval may be noted in several places upon the tracing. Pulse rate about 60 to the minute.

The attacks which had preceded the one in which I saw this man had been of brief duration, the heart maintaining the slow beat but a few hours or a day at most. This attack, however, kept up for several days, with only short intermissions. He had discovered that a strong drink of whisky would, for a time at least, bring the pulse up to normal. I saw this verified (Fig. 6). During the period of slow ventricular action the patient was able to walk only at a very slow pace, and had to be very careful not to over-

exert himself in any way, yet he travelled about alone, attending to his business affairs.

AURICULAR FIBRILLATION (THE WHOLLY IRREGULAR PULSE). This is characterized by an entire loss of the sinus or fundamental rhythm, the beats are irregular both as to time and as to volume. In the venous tracing the auricular wave is missing, in other words, there is no auricular contraction, the venous pulse being of the ventricular or positive type (Fig. 7). There is a general fibrillary contraction of the auricular muscle, but no contraction of the muscle in mass. The electrocardiagram shows an absence of the *P* wave (auricular contraction), and by a series of fine undulations that there are a number of impulses at the rate of four to nine hundred a minute trying to get through to the ventricle. Of course

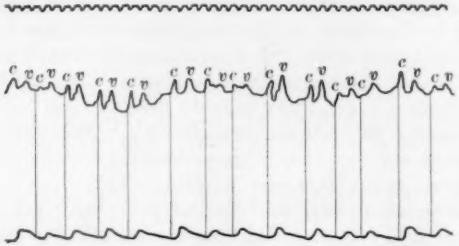

FIG. 7.—Auricular fibrillation. Note absence of *a* wave and irregularity as to time and volume of radial pulse.

the ventricle is entirely unable to respond to anything like this number, and hence responds only as it may, which results in absolute irregularity. Where a mitral presystolic murmur has been present it disappears as might be expected, it being produced during the contraction of the auricle.

PATHOLOGY OF AURICULAR FIBRILLATION. The heart muscle as a whole shows a more or less marked grade of inflammatory change resulting in fibrosis. The morbid changes are said to be particularly marked in the auricular tissue, especially at the sino-auricular junction; the same changes have been noted at the auriculoventricular bundle and in scattered areas of the ventricular musculature. Though these very decided changes have been noted in cases of auricular fibrillation, just the same conditions have been found where, during life the rhythm had been normal.

It is in this form of irregularity that digitalis has been found of the greatest value. It apparently acts by cutting down the number of contraction impulses which get through to the ventricle. The prognosis should be guarded in these cases.

THE PULSUS ALTERNANS is not properly a disorder in the cardiac rhythm as the time between the beats is the same in uncomplicated

cases, but it is not unusual to note the condition in combination with other forms of irregularity such as extrasystole.

This form of irregular pulse is seen clinically under two sets of circumstances, namely: (1) When the apparently healthy muscle is overtaxed, especially when the rate is unusually rapid, as in tachycardia, and (2) when the musculature is profoundly affected, usually by the senile changes. It is said that in those of the second class it is frequently accompanied by grave symptoms, such as pain of an anginal nature, and those who show alternation are not likely to live more than a few years. As a rule the blood pressure is high.

In conclusion I would say that the graphic study of the pulse is not only interesting to any one who will give it sufficient attention, but, in many instances, facts of importance may be learned from it. It would be extremely difficult to positively identify some sinus arrhythmias in any other way than instrumentally, and yet this might be of vital importance. There are also cases of extrasystole which could not be distinguished from auricular fibrillation by the usual methods of physical examination. A delay in the *a–c* interval may be the first indication of an impending heart-block, and when a block is actually established, none but the experienced observer would be able to identify it without instrumental assistance. As our knowledge of the causes of the individual irregularities becomes more exact, it seems fair to suppose that it will become increasingly important to be able to recognize and give them their true valuation.

While no specific reference has been made in the text of this article to Thomas Lewis' book, *Mechanism of the Heart Beat*, it is a most complete collection of the data bearing upon the whole subject as well as embodying many original observations, and is of inestimable value to those who may be interested.

CRYPTOGENETIC GRANULOMATOSIS OF THE STOMACH.

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and

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Extreme thickening of the walls of the stomach, with marked shrinkage of the organ, has been observed frequently, and has received a different name at the hands of every writer on the subject. The attempt has been made to class every example of

this type of disease under the one heading, "cirrhosis of the stomach" or "linitis plastica," regardless of the fact that the microscopic anatomy of the condition is not always the same. The most recent contribution on the subject is that by Henry H. M. Lyle,[1] who classifies the cases in the literature into benign and malignant. Some of the latter cases were characterized by the presence of "epithelial" cells lying in meshes of undulating connective tissue fibers in the submucosa, infiltration of the submucosa with fusiform cells, and endarteritis in the vessels. Lyle admitted that it was a disputed question whether these epithelial cells were really carcinomatous or whether they sprang from the endothelium lining the normal lymph spaces. In view of the changes that were noticed in 2 of our series, the fact that the adjoining lymph-nodes were usually fibrosed in Lyle's collection leads us to doubt the correctness of the view that such types of disease are necessarily malignant. Four specimens which have come under the writers' notice demonstrate the existence of certain histological types of the disease and corroborate the results of an investigation of the literature of the subject from this standpoint. It seems possible, accordingly, to classify the cases into the following three main groups: (1) Definitely cancerous cases; (2) pre-cancerous or doubtfully cancerous cases; (3) non-cancerous cases. It is the purpose of this paper to present the evidence in favor of the classification submitted.

CASE I.—Definitely cancerous. J. P., male, aged forty-eight years. Had symptoms pointing to cancer of the stomach. The autopsy showed an extensive cancer in the stomach with multiple discrete nodules scattered through it. The tissues around were infiltrated.

Histologically the mucosa and submucosa were replaced by large branching acinous masses of cells of epithelial type, separated from each other by only a scanty amount of fibrous tissue. The muscularis was not infiltrated, the carcinomatous cells spreading uniformly along the thickened walls of the stomach without passing through to the peritoneal side. Apart from the rarity of the mode of invasion of the gastric wall, the case presents no striking interest because the histological diagnosis is easy and allows of no alternative opinion.

CASE II.—E. S., male, aged forty-seven years, had suffered from epigastric pain and vomiting for six months. Vomiting came on seven weeks before admission to hospital. There was blood in the vomited matter. Liquids alone were retained. There was much emaciation.

The stomach was excised. It was a small organ, about 15 cm. in length, with uniformly thickened walls. The patient did not

[1] Ann. Surg., 1911, p. 625.

survive the operation longer than one week. The autopsy showed bronchopneumonia with extensive consolidation. There was a little peritonitis at the site of operation, and there were no infected glands.

Histological characters: The gastric glands are intact but their fundi are obscured by an excessive amount of small round-celled infiltration which spreads as far as the well-marked narrow stratum of muscularis mucosæ. Between this and the muscularis is a striking amount of submucosal infiltration (1.4 cm. in thickness). The muscle fibers of the muscularis are separated by a very dense cellular infiltration of the same type as is seen in the submucosa, and a similar change extends through to the peritoneal coat, where there is a layer of organizing granulation tissue. In one portion of the sections there are small tongue-like acini of cuboidal cells which simulate spheroidal-celled carcinoma. These occur immediately beneath the muscularis at the extremity of the section.

Characters of infiltration: The cells are large and polygonal; the cytoplasm is narrow; the nucleus is oval, pale, and finely granular in structure. Some cells are provided with a very pale structureless nucleus, while some have a broader cytoplasm. The cells are mostly of one type, and are mesolymphocytar in character. They are separated by strands of fibrous tissue at long intervals. Here and there the fibroblastic infiltration is diffuse and marked. There are very few true lymphocytes, but there are a number of lymphocytar cells mixed with eosinophiles of histiogenic type. Occasionally there are mitotic figures in the lymphoidocytar cell-types. Some of the eosinophile cells have the character of micromyelocytes. The exudate between the tubules consists very largely of cells of mesolymphocytar type intermingled with a number of plasma cells of the ordinary form. There are many other forms present, such as small lymphocytes, lymphoblasts, and myelocytiform cells. The plasma cells are most numerous near the orifices of the glands and here eosinophiles appear. There are some small, fairly well outlined lymphoid nodules just beneath the mucosa.

Case III.—A. P. L., male, aged fifty-two years. Had suffered from epigastric pain for years. Latterly he had been much worse and was now unable to retain solids. He had had ague twice, and admitted gonorrhea, but not syphilis. There was a small mass in the epigastrium. The test-meal showed absence of free HCl. The autopsy showed extreme emaciation, strong basal pleural adhesions on both sides, atheroma of the cerebral arteries, but not of the aorta. There were miliary nodules over the peritoneum, and there was ascites. The glands in the portal fissure and mesentery were enlarged. The kidneys were very cystic. The stomach was not dilated; its walls were uniformly and markedly thickened

(½ inch) from the cardiac end to within an inch of the pylorus. There was a small ulcer near the pylorus. The testes were normal.

Histological characters: The submucosa is occupied by a very edematous and cellular tissue. The gastric glands are just visible here and there, but are much obscured by the degree of cellular infiltration between them. The individual cells are considerably separated as if from catarrh. The submucous tissue contains a number of polymorphous cells with oval pale nuclei and scanty chromatin network. The cell body is very large and pale. Among them are small lymphocytes and a few plasma cells of ordinary type. There are many binucleate and trinucleate eosinophile cells. Running irregularly throughout the whole are some broad, absolutely ill defined bands of hyaline substance. The bloodvessels are scanty. This condition goes down almost uniformly to the muscularis, but the cellular content is increased as one passes in that direction. The cellular infiltration is very dense among the muscle fibres; it does not seem to displace them much. On the peritoneal side there is little or no deposit, though there are flattened delicate spindle cells running along in the form of a thin band covering the muscularis. The nodule on the peritoneum shows a loose structure of elongated spindle cells, a few polymorphs, and much edema. There is no evidence of carcinomatous change in it.

Case IV.—G. P., female, aged sixty-two years. Had symptoms pointing to carcinoma. The autopsy showed a leather-bottle stomach and infiltration of the adjacent coils of intestine by new growth, with consequent stricture of the lumen of the intestine. There were miliary nodules over the peritoneum.

Histological characters of the tissue: The submucosa is occupied by a very cellular tissue containing delicate connective-tissue fibrillæ running through it in all directions and leaving minute spaces in which lie the individual cells composing the tissue. These cells are medium in size, round or polygonal in shape, and have a regularly large oval nucleus with scanty nuclear markings, very amblychromatic and very clearly defined nuclear membrane. Some of the cells have an eccentric nucleus of small size. Very few elongated nuclei occur, showing that there is little tendency to differentiate into young fibroblasts. One or two very large cells occur with relatively preponderating cell-body. This infiltration becomes a little fibrous as one approaches the muscularis. There is very little involvement of the latter and little increase of fibrous tissue. On the peritoneal side is a little exudate which is moderately cellular, the cells being of a different type, pale, and far apart, and of more spindle shape (broad body and oat-shaped nucleus). There are a few scattered lymphocytar cells. The bloodvessels are very congested. Here and there are a few thromboses, and, in a few areas, hemorrhages occur. Another section

shows a very decided fibrosis in the submucous layers. The glandular layer cannot be seen. A third section shows some edematous portions with very wide separation of the cells, though these are relatively more numerous. Some of the larger cells appear to be vacuolated and others show mitotic figures, and others (looked at from an impressionist point of view) may be regarded as bearing some resemblance to carcinoma cells.

CASE V.—G. B., male, aged fifty-six years. Had symptoms indicative of gastric carcinoma. The autopsy showed a diffuse thickening of the gastric walls with shrinkage of the organ. No other abnormal points were noted.

Histological characters of the tissue: The wall of the stomach is entirely occupied by new tissue. There is a small relic of muscular tissue. The mucosa itself is replaced by cellular tissue which is very thick (1.5 cm.). In one or two places there are some thick-walled bloodvessels, but the bulk of the tissue is almost avascular. There are irregular strands of fibroblastic tissue which vary in thickness. Here and there in this tissue there are just sufficient spindle cells to give it a fibrous appearance, otherwise it consists of necrotic or fibrotic interstitial substance in which lie large round discrete cells with very trachychromatic nuclei and relatively scanty dusky basophile cytoplasm. Among these there are a few very large cells with lobed nuclei simulating the metrocytes found in bone-marrow. Others have a more oxyphile cytoplasm with a nucleus in which no structure can be discerned. Many examples are in a state of amitosis. In addition there are cells of the size of mesolymphocytes with a relatively scanty cytoplasm. A moderate number of small round cells like ordinary lymphocytes can be seen. Necrotic areas occur here and there. They are small, irregularly shaped, and contain a few fragmentary nuclei of punctate form up to the size of an ordinary lymphocyte nucleus. These areas strongly recall those seen in acute streptococcic infections. In between the strands referred to there are ill-defined collections of small round cells which are separated by a more or less abundant reticular connective tissue and include very many densely trachychromatic lymphoid cells. A few larger cells occur here and there, presenting a type of plasma cells. Eosinophiles are not noted at all.

A second section shows patchy infiltration between the muscular bundles, and the tissue is everywhere looser in texture. Short spindle-shaped cells and small round and polygonal cells being intermingled with the larger cells of the types described above. Many lines of fibrous tissue are more conspicuous here than in the other section. A few cells occur which contain cell-inclusions.

The last of these cases appears to be essentially distinct from the others, the difference consisting in the abundance of large, atypical, uninucleate giant cells which occur in groups through the

tissue. These groups are not acini but are collections of cells which have no very definite relations with each other and are of an endothelial type, suggestive of their connection rather with fibroblastic metaplastoid tendencies. We have not found more than one case in the literature, either in the references presented by Lyle or in certain other references quoted at the end of this article, which is at all comparable with the particular condition which we have classed at the outset as non-cancerous.

This case is reported by Johnston,[2] and occurred in a boy, aged thirteen years, who only weighed thirty-seven and one-half pounds. The stomach measured 5 by 2.5 cm., and its walls were free from 0.8 to 1.5 cm. thick. There was general lymphadenitis. There was a small ulcer at the pylorus. The mucosa was everywhere lost except toward the pylorus, where fragments were still discernible. The muscle fibers were separated by vascular connective tissue, in which there was a variable amount of small round-celled infiltration. Among these inflammatory cells plasma cells were noted in abundance. Ganglion cells were numerous in the walls of the upper portion of the stomach but less numerous in the lower portion. These cells were large, and occurred in groups and were surrounded by connective tissue, and took a darker stain than the surrounding cells. There was no evidence of carcinoma anywhere. The vessels were frequently plugged by thrombi. The peritoneum was uniformly thickened over the ulcer and there was marked round and plasma cell infiltration of all the tissues of the wall at this spot as far as the peritoneal surface. There were no pathological changes in the wall of the duodenum.

The character of the tissue itself is quite characteristic; it has all the indications of granulation tissue of chronic type. In other words, an observer, not knowing the source of the tissue, would suppose it to be a granulomatous mass similar to that produced by mycotic infection. The peculiarity is that the change has extended uniformly along the whole organ. Those who, with Krompecher, regard the condition as secondary to a chronic venous stasis provide an explanation for a chronic toxic agent, acting over a long period of time, stimulating the connective tissue cells to multiply in this fashion. Granuloma formation elsewhere is attributable to a toxic agent acting over a long period of time.

According to Boas,[3] the cirrhotic condition of the gastric wall is due to chronic spasm of the muscles. Such an explanation is rarely borne out by the microscopic characters of the muscular coat.

Much depends on the interpretation which is to be placed upon the so-called epithelial cells. Where they occur diffusely and intermingle without fibrous boundaries with inflammatory cells of all kinds, such as occur in a chronically inflamed tissue or a

[2] Trans. Chicago Path. Soc., vi, 336.

[3] Deutsch. med. Woch., 1902, p. 170.

healing or organizing granulation tissue, they are probably really nothing more than hypertrophic or actively multiplying connective-tissue cells or adventitial cells, and are not at all neoplastic in nature. It is only in those cases where they form definite acini demarcated by a capsule of more or less well defined fibrous tissue that the diagnosis of carcinoma can be maintained. The occurrence of a few packets of cells, unless they present very characteristic cytological features, cannot be held to be conclusive of malignancy. The similarity to this type of cell, which is presented by the hypertrophic ganglion cells in the gastric wall, is also very suggestive of error having arisen in the description of certain cases.

For these reasons we would be disposed to assume that in some of the doubtful cases of the literature, for example, Stretton,[4] Grooves,[5] Nuthall and Emanuel's,[6] Kussmaul's and Schirren's, we have before us examples of the third type of cirrhosis of the stomach, that which simulates granulomas of known etiology. In the present instance, as especially exemplified by the fifth case which we report, the similarity to some other granulomas of other obscure origin, would make it suggestive to place it in a similar group. Since its etiology is unknown, though probably toxic in nature (not syphilitic) it may be called a cryptogenetic granuloma. Since the condition is diffuse the term granulomatotic hyperplasia better describes the appearances, and emphasizes the diffuse character of the disease. Furthermore, this enables the local type of cirrhosis of the stomach to be excluded from the classification because the thickening is here due to pure fibrosis without the occurrence of any small-celled infiltration; for example, Tilger's[7] case.

As regards the relationship of the granulomatous change to carcinoma, it may be pointed out that the presence of a few acini of apparently cancerous cells, in the midst of or at the edge of a massive inflammatory tissue, hardly justifies the conclusion that linitis plastica is primarily malignant. There is no reason why a small nodule of spheroidal-celled carcinoma in one spot, generally near the pylorus, should excite a widespread fibrosis extending along the whole surface of the stomach. A similar condition is unknown in any other part of the body. The analogy to the carcinomatous change appearing in a lupus or in a tongue along the seat of chronic interstitial syphilitic glossitis is suggestive. On the other hand, it is not possible to state that Case V would not have developed cancerous acini if life had been prolonged.

The fact that some of these cases have been described as sarcoma brings up the problem of lymphosarcoma versus lymphogranuloma, a problem which has arisen in connection with new

[4] Lancet, 1909, p. 465.
[5] Practitioner, 1905, lxxv, 172.
[6] Trans. Path. Soc., London, 1903, p. 90.
[7] Virchow's Archiv, Band cxxxii, p. 290.

formation of tissue in other parts of the body. According to Naegeli,[8] Ribbert,[9] and others, the formation of a lymphosarcoma, resulting from purely parenchymal hyperplastic processes, is distinct from the formation of a granuloma where there is an interstitial proliferation associated with the parenchymal change. The other school of hematologists, following Pappenheim,[10] bring these processes into closer relation by regarding them both as variants of lymphosarcomatous development. It is more satisfactory to look upon these processes as related in this latter way, because it affords an explanation for the possible change between the one form of disease and the other. The noxa which stimulated the abnormal proliferation of potentially hematopoietic cells may or may not also irritate the purely stromatic cells and lead to the histological picture of a lymphosarcoma or of a granulomatous tissue (one form of linitis plastica) respectively. The view that it is an irritant which starts the whole process renders it more intelligible why one should meet with cases which run diffusely through the gastric wall alone, and sometimes with cases which run through the intestinal walls as well. From the description of such cases as are available it is impossible to escape the conclusion that the so-called "diffuse carcinoma" is really a form of lymphosarcoma with more or less conspicuous involvement of the purely connective-tissue cells. A good example of the purely lymphosarcomatous hypertrophy of the gastric wall which was very extensive though not general through the whole stomach was reported by one of us[11] recently, and brings out the contrast between the two conditions as well as a demonstration of the possible interchangeable character of the lesions according to the preponderance or otherwise of the interstitial hyperplastic phenomena. This possibility is further shown by those few cases of "malignant granuloma" which have occurred in this hospital during recent months, where there was in addition a megakaryocytar hyperplasia with the production of a very characteristic histological picture.

The introduction of these three forms of disease in a commentary on the cases of linitis plastica which are in question serves to explain the view that each of these three processes may represent different modes of action of one group of etiological factors. The view that slightly different histological manifestations can result from one and the same causal agent has been advanced by Pappenheim, in 1909, who gave arguments for believing that a toxic infective agent could set up granulomatous and leukemic processes on the one hand and lymphosarcomatous processes on the other, and that some lymphosarcomatous growths could arise under different conditions still, conditions in which an infective agent had no part.

[8] Blutkrankheiten, 1908.
[9] Allgemeine Path., 1909.
[10] Folia Hæmatologica, 1907, pp. 244 and 246.
[11] Gruner, Canadian Pract. and Rev., March, 1912.

To summarize the ideas above expressed, in so far as they bear upon the linitis plastica, we arrive at the conclusion that this disease is not a new kind of morbid process, but is the effect of some chronic infective agent whose nature has not yet been determined. The process at work is often akin to the granulomatous process which occurs in mediastinal tissues and elsewhere, it is akin to the changes which occur in the course of some forms of tuberculosis and of diffuse sclerotic types of tertiary syphilis, and it is occasionally followed by the development of an epithelial growth, just as is sometimes noticed as a sequel to tuberculosis and syphilitic lesions.

The disease known as linitis plastica, or cirrhosis of the stomach, only demands a separate name because it is clinically a simulator of true carcinoma. Its prognosis should be more favorable and its treatment by the surgeon more effective.

It is further worthy of mention that the small degree of epithelial overgrowth which may be regarded by some observers as carcinomatous, in Cases II, III, and IV of our series, are not really any greater in extent than are the atypical proliferations of epithelium which are known to result from the subcutaneous introduction of certain irritant lipoid soluble bodies. The suggestion is that the abnormal cells in this granulomatous tissue are pouring out substances which may excite the overgrowth of the glandular epithelial cells in the same way that many bodies (dimethylamidoazobenzol, amidoazotoluol, α-naphthylamine, methylimidazol, indol, and skatol, etc.) were found to excite epithelial overgrowth by Wacker and Schmincke[12] in 1911. This renders the development of carcinoma as a secondary process on a preëxisting (often long-persistent) submucosal disease quite intelligible, and emphasizes the view which we would point out that the malignant change in this, as in "Hodgkin's disease," and in many lymphosarcomas (also in Paget's disease of the bones), is not an inevitable sequence, but is superimposed by the succumbing of certain other tissues to the continued noxious action of abnormal cell-products.

THE ALIMENTARY HYPERSECRETION OF CHRONIC ULCER AS SHOWN BY THE LACTOSE TEST MEAL.[1]

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Considerable data must be collected before the causation of anomalies of gastric secretion will be entirely understood. Much

[12] Münch. med. Woch., 1911, p. 1607.

[1] Read before the American Gastro-enterological Association, June 3, 1912.

of the literature on the subject was written when clinical pictures were differently interpreted from the way they are today. The relation between stomach symptoms and diseases of other organs was little appreciated previous to the present decade. Chronic peptic ulcer was an almost unknown disease. Methods of diagnosis have gradually been improved, and entirely new methods have been originated.

The literature concerning gastric secretion following the ingestion of test meals is meager and unsatisfactory. With the ordinary test-meals in vogue it has been impossible to gain any notion of the constitution of extracted chyme. As a routine, we have been most concerned with the presence and percentage of free acid and the total acidity. Sahli and Friedman have each proposed a test-meal containing fat which was to be used as an index of the amount of the chyme made up of test-meal residue. Little clinical work with these methods has been reported.

Last year at the meeting of the American Gastro-enterological Association, I urged the advantages of a test-meal in which lactose was used as an indicator. Let me briefly recall the composition of this meal and its method of use, referring to the original article[2] for necessary details. The test meal consists of 300 c.c. of weak tea or water to which is added 30 grams of lactose. With this the patient takes two unsalted, unsweetened crackers. At the end of an hour a portion of chyme is extracted, and then a definite amount of water, for example, 150 c.c., is injected through the tube and mixed with the chyme by partially withdrawing it and forcing it in again. From the difference in the acidity of these two samples the total stomach content is calculated by the formula suggested by Mathieu. The lactose percentage is then accurately determined in the first or undiluted specimen, and from that we determine the amount of sugar remaining in the stomach, and calculate the amount of the chyme which is made up of test-meal residue, and that which is made of gastric secretion.

During the last year I have continued the daily use of this test-meal, and have been convinced of its accuracy and the importance of the obtained data. Repeated tests in the same individual show that the results are consistent. Its accuracy in the estimation of the motor power of the stomach has been corroborated by Röntgenoscopy when used as an aid to diagnosis. In no thoroughly studied case have we been able to contradict that it gives an accurate idea of the motor power of the stomach for fluids. The question arises as to the accuracy of estimation of gastric juice secretion. Unfortunately, we are lacking in practical methods to verify the results, but from our studies we have no reason to question their accuracy.

[2] Jour. Amer. Med. Assoc., March 16, 1912, lviii, 753.

We know how much test-meal has passed out of the stomach from what remains, and the question remains as to whether a proportionate amount of gastric juice has passed over. This problem is difficult of solution, as we have no means of knowing that in the hour of the test conditions are at all times the same as when an hour has expired. In the same case, tests taken at periods after the ingestion of the test-meal, varying from ten minutes to one hour, indicate that gastric secretion begins promptly after this test-meal; free acid is soon present, and even in ten minutes the stomach may contain from 50 to 100 c.c. of gastric juice. If it be true that the rate of gastric juice secreted and passed from the stomach corresponds proportionately with the test meal evacuated, there must be wide deviations in the amount of secretion, and, in certain cases, the amounts must be very great. This is a matter of much practical interest.

An idea of the amount of secretion is gained by the ratio which obtains between the test-meal residue and the gastric-juice residue. Thus, if we find 50 c.c. of test meal and 100 c.c. of gastric juice in the stomach, the ratio is 1 to 2. If the rate of exit of the two is constant, then, using the same example, the amount of gastric juice passed out would be 250 times 2 or 500 c.c. of secretion passed and 100 remaining. These figures are not surprising when we stop to think how large is the amount of gastric juice produced by a fractional part of the canine stomach, studied with the Pawlow method.

In order that we may appreciate the results obtained in chronic ulcer, it will be necessary first for us to fix in mind the figures for cases which have been selected as normal and those where certain definite conditions have been discovered other than the one under consideration. A large number of cases have been studied in search of possible gastric derangements and for statistical purpose. From these I have selected 10 which appeared to be within the normal limits of motility and secretion. Not every case, experimentally studied, proved to be as normal as its freedom from complaints might seem to indicate. This is, it seems to me, a thing we should expect.

TABLE I.—Normal Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	19	40	30	47	1 to 1.6
2	34	55	33	80	1 to 2.4
3	20	60	34	50	1 to 1.5
4	30	50	35	81	1 to 2.2
5	32	47	45	85	1 to 1.8
6	16	54	29	80	1 to 2.8
7	32	44	24	41	1 to 1.7
8	20	40	26	31	1 to 1.2
9	30	50	35	80	1 to 2.3
10	10	41	50	97	1 to 1.9

There is little use in prolonging this table for normal cases, as the standard is necessarily more or less arbitrary. I regard the above figures as within the normal limits. We may say that more than 50 c.c. of test-meal residue shows deficient motility, and that the ratio of test-meal residue to gastric-juice residue should be about 1 to 1½. If the two are equal, or the gastric juice less than the test meal, there is deficient secretion. I would not place the upper limits of this ratio with an equal degree of positiveness. The question presents itself as to whether symptoms or pathological digestion arise, as a rule, when the ratio reaches a certain figure. It will take a deal of study and clinical observation to determine such questions.

TABLE II.—Enteroptotic Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	18	42	84	60	1.4 to 1.0
2	10	35	85	68	1.4 to 1.0
3	16	42	123	41	3.0 to 1.0
4	8	28	216	150	1.4 to 1.0
5	9	26	191	104	1.8 to 1.0
6	34	60	15	44	1.0 to 2.8
7	30	50	57	76	1.0 to 1.3
8	0	12	205	195	1.1 to 1.0
9	0	18	40	30	1.3 to 1.0
10	0	12	34	48	1.0 to 1.3
11	10	26	62	102	1.0 to 1.7
12	0	12	32	48	1.0 to 1.5
13	30	46	47	47	1.0 to 1.0

In order to give some idea what takes place in the general group of cases spoken of as enteroptotics we have compiled Table II. It is apparent that in the main these cases are characterized by some degree of motor insufficiency. In some cases the motor capacity for fluids is fair or even excellent. In quite a large proportion the secretion is low. In this type of case it rarely appears high. Case 8 in Table III is shown to have a fair degree of hypersecretion. In this case there was a marked enteroptosis.

TABLE III.—Chronic Appendicitis.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	22	41	75	105	1.0 to 1.4
2	60	76	25	86	1.0 to 3.2
3	12	32	85	60	1.4 to 1.0
4	20	44	75	106	1.0 to 1.4
5	34	60	59	103	1.0 to 1.7
6	50	65	51	120	1.0 to 2.3
7	20	35	28	84	1.0 to 3.0
8	44	64	43	75	1.0 to 1.7
9	12	30	101	80	1.2 to 1.0
10	0	18	40	33	1.2 to 1.0

These cases were all explored and the sole lesion was a chronic appendicitis. In Cases numbered 1, 6, 7, 8, there was epigastralgia of severe grade which ceased after appendectomy. From the marked difference in the degree of acidity and gastric juice in these cases it would seem doubtful that the acid secretion caused the pain, either directly or through inducing pylorospasm. In Cases 2 and 8 there was hunger pain relieved by alkalies and the ingestion of food. The high secretion in these cases may have been a factor in the causation of the discomfort.

TABLE IV.—Gall-bladder Diseases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	30	50	80	90	1.0 to 1.1
2	44	72	31	67	1.0 to 2.2
3	28	40	211	142	1.6 to 1.0
4	0	15	65	65	1.0 to 1.0
5	0	13	112	53	2.0 to 1.0
6	38	51	57	84	1.0 to 1.4
7	8	32	33	44	1.0 to 1.3

Gallstones were found at operation in the first 3 cases. In the other 4 considerable observation has justified a positive diagnosis of gall-bladder trouble, but operation has as yet been refused. Test-meal studies have not been necessary in the majority of our cases, as the diagnosis was sufficiently clear to allow the recommendation of operation unhesitatingly. In the cases reported the nature of the complaints was such as to make differential diagnosis between a gall-bladder disease and other abnormal conditions somewhat difficult. The results of the test meal were of great value in reaching conclusions, particularly in Cases 1 and 3. Here there was epigastric hunger pain relieved by food. In Case 3 there was a hematemesis after prolonged vomiting, but exploration showed no ulceration.

TABLE V.—Ulcer Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	56	80	36	149	1 to 4.0
2	66	80	34	136	1 to 4.0
3	46	68	55	224	1 to 4.0
4	44	65	20	150	1 to 7.0
5	36	50	37	130	1 to 3.7
6	46	60	64	212	1 to 3.4
7	80	120	15	138	1 to 9.0
8	38	50	38	119	1 to 3.2
9	36	61	10	94	1 to 9.4
10	20	44	36	139	1 to 3.7

It is obvious that in this group of cases there is a decided tendency to alimentary hypersecretion. (There is the question of the correctness of the diagnosis, sometimes admittedly a difficult

matter.) Only the first 2 cases have been submitted to operation, and in both there was duodenal ulcer. In Cases 4 and 5 there could be no doubt of the diagnosis, as there was marked overnight stasis. The diagnosis in the other cases had been made on the history and *x*-ray findings, previous hemorrhage and occult bleeding when first studied.

To the above cases of ulcer 2 may be added upon whom gastro-enterostomy was performed before test-meal studies of this kind were instituted. Operation did not result in entire relief of symptoms.

TABLE VI.—Unsuccessful Gastro-enterostomies.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
11	16	32	38	124	1 to 3.2
12	17	35	11	69	1 to 6.0

The consistency of results in repeated observations on some of these ulcer cases is shown by the following figures where cases have been under medical treatment.

TABLE VII.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
2	34	136	1 to 4.0
	49	120	1 to 2.4
	26	162	1 to 6.4

Benefit in subjective symptoms had apparently resulted when the second test meal was taken. An exacerbation of symptoms at the time of the third meal made operation advisable.

TABLE VIII.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
3	55	224	1 to 4.0
	46	187	1 to 4.0
	21	113	1 to 6.0
	52	115	1 to 2.2
	55	137	1 to 2.3
	22	128	1 to 5.0
	41	71	1 to 1.8
	44	105	1 to 2.4
	42	118	1 to 2.7
	51	120	1 to 2.3

This case, under medical treatment, has suffered the usual remissions and exacerbations, refusing radical operative treatment. The test meals have been taken during the last year. For the last four months the patient has been free from symptoms, and during this period the last four meals were examined.

TABLE IX.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
4	20	150	1 to 7.5
	22	178	1 to 8.0
	16	99	1 to 6.0
	40	110	1 to 3.0

This case is interesting in that it shows that although there is pyloric stenosis, as shown by large overnight stasis of rice and rasins, the fluid test-meal residue may be small. Operation was refused and the lowering of the secretion ratio followed diet, medication, and systematic lavage. There was marked improvement in subjective symptoms corresponding with the fall of gastric juice secretion.

CONCLUSIONS. The demonstration of an alimentary hypersecretion is strongly suggestive of a chronic gastric ulcer. Whether a low ratio occurs in a case of ulcer of this type must be determined by future observations. How frequently alimentary hypersecretion occurs in conditions other than ulcer cannot be stated on this comparatively small number of studied cases. In a few instances we have found the gastric juice three times the amount of the test-meal residue. A ratio as low as this has proved the exception in those cases in which ulcer has been diagnosticated.

INTERMITTENT SPINAL CLAUDICATION.

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INTERMITTENT claudication may be divided into (1) the cerebral type, (2) the peripheral type, (3) the lumbar type, and (4) the spinal type. The arteries most commonly involved are the tibial, brachial, coronary, mesenteric, cerebral, and spinal arteries.

The chief cause is arterial disease, arteriosclerosis, senile calcification, obliterating endarteritis, acute arteritis. Not only are there organic changes in the vessel walls, but also an associated vasomotor neurosis, with a tendency to vascular spasm, which narrows the lumen of the vessels and diminishes the flow of the blood to the parts, with a resulting ischemia. Oppenheim recognized a benign purely functional type due to vascular spasm. Venous changes or diseases may give rise to symptoms of claudication similar to those in case of arterial disease. A secondary change follows in the nerve trunks and fibers as would be expected from impaired nutrition.

The predisposing causes are: (1) Exposure to cold and wet involving the anterior and posterior tibial arteries, (2) use of tobacco (Erb), (3) occupations such as that of marble-cutters who use the pneumatic chisel, and (4) senility. The exciting causes may be grouped under: (1) Syphilis, (2) acute infections, as influenza and acute endocarditis, and (3) alcohol.

It was shown in Charcot's[1] original observations in 1858 that with involvement of the large arteries of the lower extremity, intermittent limping, weakness, painful cramps, and paresthesia may develop in the extremities while walking, disappearing after a period of rest (paralysie douloureuse intermittente). The peculiar feature of this is the intermittent character of the symptoms, their appearance only during muscular activity, and their rapid disappearance in the passive state.

Erb,[2] in 1898, showed that more frequently the smaller ramifications of the arterial tree are involved with corresponding changes in the pulsations of the pedal arteries.

Williams[3] has reported a case of intermittent claudication involving an upper extremity. When the condition affects the upper extremities it is accompanied by numbness, the parts being cold, white, and painful, and resembling greatly one stage of the picture presented by Raynaud's disease. By resting and rubbing the hands the symptoms disappear. Frequently those afflicted in this way are obliged to change their occupation.

J. Ramsey Hunt[4] has recently described in a graphic manner the lumbar type of intermittent claudication. In this there is severe pain in the lumbar region, intermittent in character, occurring regularly during activity and ceasing after a short rest. A sufficent amount of blood is supplied during the passive state, which does not suffice, however, for the increased demand of the sacrolumbar mass during activity, hence the painful cramps and their peculiar intermittent character.

J. Dejerine[5] has described the type of intermittent spinal claudication. He states that the diagnosis from peripheral intermittent claudication depends on the absence of pain and circulatory disturbances and the presence of vesical and rectal symptoms—the condition being one of defective blood supply of the lumbar enlargement. The disorder is more common in males, one side being nearly always affected sooner than the other. The course may be rapid or insidious, but all cases tend to go on to spastic paraplegia if untreated. The organic reflexes are affected from the beginning. The most common symptom being precipitate micturition. The

[1] Compt. Rend. et mém. de la Soc. de Biol., 1858, xii, 225.
[2] Deut. Zeit. f. Nervenheilkunde, 1898, Bd. xiii, S. 1.
[3] Jour. Nervous and Mental Disease, May, 1912, xxxix, No. 5.
[4] Amer. Jour. Med. Sci., February, 1912, cxliii, 2, 173.
[5] Rev. Neurologique, 1906, No. 8.

Babinski sign is usually if not always present. The ensuing paraplegia may resemble a hemiplegia, as the unequal affection of the two sides is common. The cause of the symptoms must be defective blood supply of the lumbar enlargement, as a result of which only sufficient blood is received for the physiological processes in the passive state, the supply being inadequate for the increased demands during activity. As there have been no cases of intermittent spinal claudication reported in the English language, so far as I know, I feel warranted in presenting these 2 cases:

CASE I.—T. B., aged forty-three years, married, native of Ireland. He was first seen September 10, 1910, and complained of weakness in his left leg and burning sensation and pain in the lumbar region of the back.

History of Present Illness: He noticed weakness in both legs three years ago; this came on suddenly while he was cutting grass. He was told he had sciatica. He continued working, but was compelled to stop from time to time on account of weakness and stiffness in his legs. The condition seemed to be worse in bad weather, and when he did a great deal of walking. He had a burning sensation in his back and at times cramp-like pains.

Past Medical History: He had the usual diseases of childhood, typhoid fever when aged twenty-one years, pneumonia at twenty-two.

Social History: He used alcohol to excess until three years ago. All venereal history is denied.

Family history is negative.

Examination of patient showed the pupils to be equal. Irides responded equally and well to light and accommodation. The knee-jerks were exaggerated. Both legs were spastic, but the left was more so than the right. No clonus was observed. There was slow hyperextension of the great toes when the soles of the feet were stroked (Babinski). No sensory changes were obtainable in any part of the body. Muscular power was somewhat impaired in the left lower extremity. Slight atrophy of the thenar and hypothenar eminences was observed on the left side. The arm reflexes were all exaggerated, with the possible exception of the right biceps.

The patient came under my observation March 19, 1912. A diagnosis of intermittent spinal claudication having not as yet been made. From him I elicited the following: In January, 1912, he fell and broke his right humerus. Since then his left leg has been weaker and has bothered him considerably. When walking suddenly all power leaves the left leg and he falls unless he immediately receives some support. In a few minutes the power returns and he is able to go on his way. Some of the muscular power leaves his left arm when the leg gives way, and his left foot becomes cold. As the foot becomes warmer his leg feels better. He has good use

of his right leg, but it becomes a little cold at times. On an average of once a day he has attacks in which his left leg jerks, the leg being flexed on the thigh, and is drawn up forcibly. The great toe moves backward and forward. This takes place lying or sitting; but if he gets up and bears some weight on the leg these movements stop. If he bears much weight on it, the leg suddenly gives way and he falls. Sometimes his back also feels weak, especially when the leg gives way. The left foot, when the attacks of weakness occur, feels as though it were swollen, but when examined it is found to be normal. Once in a while his left hand feels clumsy and he is unable to pick up various articles. In a short time this passes away and it feels normal.

After lying down and on awaking in the morning he can urinate with ease; however, during the day when up and around he has to stop and wait until the urine comes, then it dribbles, stops, then starts again, and the flow is fairly good, but he has some trouble in voiding the last few drops. The bowels are constipated. His leg always feels worse before a change in the weather, but after the change takes place it again improves. At times he has considerable itching on the sole of the left foot. At times the left leg and left arm are weak irrespective of each other.

In the physical examination the following facts are prominent: Eyes are normal. Throat is normal. There is no noticeable change in facial muscles and no impairment of sensation in the face. Thorax is normal. Heart and lungs are normal. Abdomen is normal. There is no impairment of sensation.

Dorsal Region: He complains of a sense of weakness in the region of the second lumbar vertebra. There is no impairment of sensation about the genitalia and anus.

Left Upper Extremity: Normal with the exception of numbness, which occurs in attacks daily, radiating from the shoulder to the fingers. Never any pain.

Right Upper Extremity: Negative.

Right Lower Extremity: Patellar reflexes are prompter than normal. In testing for the Babinski there is a slight hyperextension of the great toe when the sole of the foot is stroked.

Left Lower Extremity: There is moderate impairment (changeable in character) of muscular force and power. Muscles are somewhat poorly developed. He has considerable rigidity at times; this is not noticed when the patient has been in the supine position for some time, but is noticed after waking. There is no impairment of tactile, pain, heat, cold, and deep pressure sensations. At times he has the sensation of a drop of water running under the skin and suddenly bursting. There are no apparent tremors. Movements are free in all directions. At times the leg is as if dead, and if the patient desires to cross his knee with this leg, it must be lifted over. Patellar reflexes are exaggerated; this exag-

geration varies and is more striking if tested after walking. The quadriceps extensor group can be seen contracting. He has no ankle clonus. There is a moderate amount of incoördination (heel to knee test). In testing for the Babinski there is a moderate hyperextension of the great toe when the sole of the foot is stroked. He had burning sensations in the left inguinal region two years ago, and not since.

The lower extremities were tested for changes in pain, and thermal sensations after exercise, but there was no impairment.

Gait: The patient holds the left leg as if stiff, and there is very little movement at the knee-joints in walking; the heels scrape on the ground.

Romberg's sign is negative.

Urine and blood examinations are negative.

X-ray examination of the spinal column is negative.

Wassermann reaction is negative.

Blood Pressure: Systolic, 90; diastolic, 50.

CASE II.—J. W., aged forty-seven years, druggist.

His chief complaint is pain in the back, and in walking down steps he has severe pain in the knees. After walking for a few minutes his legs become stiff and powerless, and they drag, so that he must stop for a few minutes and rest, then he can proceed as at first. His present condition began in November, 1911, when he had pain in his back and general weakness. No venereal history is obtainable. He averages one alcoholic drink daily, and uses tobacco moderately.

Physical Examination: Pupils are unequal, the right being larger than the left, and somewhat irregular in shape. They react poorly if at all to light, but react to accommodation. Some slight swaying is present with eyes closed. Gait is spastic in both legs. Reflexes of the upper arm are slightly exaggerated. Power and motion are good. Legs are somewhat below normal in strength. Upon exertion he has violent trembling of his legs. Reflexes are all greatly increased in the lower extremities, but there is no ankle clonus. Doubtful Babinski is present in the left extremity. Some slight hypesthesia in indifinite areas is found in the lower extremities. Dorsalis pedis artery is not palpable on either side. Pulse (radial) is feeble and irregular. Some myocardial insufficiency is observed.

This case was seen in the medical dispensary of the University Hospital.

In conclusion, I desire to extend my thanks to Professor William G. Spiller for his kindly interest in this paper.

THE METASTASIS OF HYPERNEPHROMA IN THE NERVOUS SYSTEM: JACKSONIAN EPILEPSY CAUSED BY SUCH LESION.[1]

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AND

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That tumors of the adrenals may exist without causing any symptoms is well known, and that metastasis of such tumors may occur in parts of the body remote from the adrenals, without previous or coincident manifestations of disease in the adrenals, is equally well known. The neurologist has small encounter with hypernephroma metastases. Its occurrence in the central nervous system is uncommon. Occasionally, he has to distinguish bone metastasis of it from brachial, pelvic, and other forms of neuralgia, but even this is of rare occurrence.

We have recently had a case of Jacksonian epilepsy, which was found to be dependent upon a metastasis of hypernephroma. The case presents many interesting features, not the least of which is the extraordinary absence of objective signs to indicate the existence of extensive and advanced disease.

The patient was a Bohemian cigarmaker, aged forty-five years, who maintained that aside from an attack of rheumatism, which he had when he was aged forty-one years, he had not been ill since childhood, until he had an attack of unconsciousness four months before he entered the Neurological Institute in July, 1911. The first attack came on suddenly while he was at work, May 9, 1911. He felt a twitching of the left thumb and forefinger, followed by a sensation of numbness and tension, gradually extending up to the shoulder, and then he lost consciousness. Within an hour he felt quite well again, save that he was weak and discouraged. Five hours later he had a second attack, but without loss of consciousness. A few days after this experience he began to have attacks characterized by paresthesia in the left hand and forearm and twitching of the thumb and index finger, which were not accompanied by any disturbance of consciousness, and which were not followed by any loss of dexterity. He had had from one to five such attacks every day for three months following the original attack. The next severe attack that he had was July 13, 1911, he being at that time in the hospital. He had two severe attacks in one day, each lasting about fifteen minutes, and each followed by

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a profound sleep. The attacks were typical of Jacksonian epilepsy, the attack beginning as above described and followed by generalized convulsions. A physical examination at this time failed to reveal any signs of organic disease of the brain, nor did the patient complain of any symptoms, save those that have been enumerated. There was no headache, vertigo, disturbance of equilibrium, loss of power in any of the extremities, or disordered function of any of the special senses. He complained only of general weakness, loss of flesh, and of the attacks of twitching or convulsions in the left hand. The attacks were not always the same. At times the sensation in the hand was that of pins and needles, and the twitching might be so slight as to flex only the thumb rhythmically a few times. At other times the sensation in the fingers and hand, wrist, and forearm was of tingling, numbness, tension, and bewilderment, and the motor symptoms were correspondingly greater. The duration of the attacks was from a few seconds to several minutes. He gave up his work because of the frequency of the attacks, and because he felt generally weak. Moreover, the left hand was awkward and weak. He remained in the hospital for one month, during this time he had no major attack, save the one mentioned above.

He reëntered the hospital September 12, 1911. He had by this time developed the only symptom which, aside from the Jacksonian attacks, he ever developed—namely, mild somnolency. He had likewise developed a physical sign which was striking. The left hand, as he lay in bed, assumed a semi-flexed position, with the thumb extended. The hand had the appearance of being atrophied, though no distinct atrophy could be made out; he could move the fingers freely and readily.

Physical examination showed moderate weakness of the left side of the body, upper and lower extremity, and face. The tendon jerks of the left extremities were livelier than those of the right. There was no Babinski phenomenon and no clonus. The abdominal and epigastric reflexes were elicitable on both sides, those on the right side being somewhat livelier than those on the left. There was slight incoördination of the left hand and a distinct impairment of dexterity of this hand. Tactile sensibility, contact sensibility, and pressure sensibility were unimpaired. He did not interpret quickly and correctly postural sensibility in the left hand, forearm, and arm. On several occasions there was distinct astereognosis of the left hand. This symptom, however, was not constant; it would be found one day and not the following day. Wassermann examination of the blood and cerebrospinal fluid was negative. The fluid obtained by lumbar puncture showed no excess of globulin, one cell, and it reduced by Fehling's solution. No abnormality of the thoracic and abdominal viscera could be made out, save that the heart was dilated, its impulse feeble, its sound puerile. The

pupils were circular, equal in size, and reacted promptly to light. The only definite physical sign that existed was an absence of the left plantar reflex.

In the latter part of September an entirely new clinical symptom showed itself in the left hand. This consisted of a rhythmical movement of the thumb and index finger, two or three short adductions of the thumb and index finger, followed by flexor movement only of the index finger and thumb. The first or coarser movements were at the rate of one per second, the slighter at the rate of eight per second. The patient was quite conscious of the movement and experienced considerable discomfort from it. This later manifestation was not accompanied by, or associated with, paresthesia, but since the onset of it the localized convulsions in the hand and forearm became more frequent, sometimes occurring as often as every half-hour. It was also noted that the tendon jerks in the left upper extremity had become much exaggerated since the onset of the rhythmical movement. Although the left hand still had a fair amount of strength and the fingers and hands could be moved, he now complained of a sense of great clumsiness in his hand, and postural sensibility became much impaired. He also complained of severe pain in the back of the hand and wrist; he could not further particularize it. There was no disturbance of contact sensibility or thermal sensibility. The patient had no symptoms of increased intracranial pressure save the somnolency above mentioned. On September 26 it was noted that the rhythmical movement of the thumb and index finger was less in intensity and frequency. At this time the rate was fifty to the minute. On September 25 it was noted that he had three major attacks three hours apart, each of which lasted ninety seconds. The rhythmical movement ceased for one-half hour after each attack. On both of these dates and on September 28 it was recorded in the clinical notes that there was no astereognosis.

Five months after the initial symptom—namely, on October 1, the patient, while lying in bed, had a series of convulsions and died.

To recapitulate: A man, aged forty-five years, who had been in good health developed typical Jacksonian epilepsy, displaying itself by twitching of the left thumb and index finger, paresthesia of the left hand, and forearm and followed on five occasions by loss of consciousness and generalized convulsions. Gradually there developed loss of power and of dexterity in the left upper extremity and to a slight degree in the entire left half of the body. The only definite physical signs were loss of sense of position in the left hand and fingers and absence of the left plantar reflex. There was an inconstant astereognosis of the left hand and a mild increase of the tendon jerks of the left half of the body. A week before his death a slow rhythmical tremor of the left thumb and

index finger, consisting of adductor movements about one per second, developed.

When the abdominal cavity was opened a large whitish tumor was found in the right flank. This tumor had invaded the upper pole of the right kidney, surrounded the adrenal and extended into the under surface of the right lobe of the liver. In various other parts of the liver there were a few metastases up to three-fourths of an inch in diameter. In the wall of the duodenum, near the junction with the jejunum, was a small metastasis one-eighth of an inch in diameter. The only other metastasis found was in the right cerebral hemisphere. This metsatasis was one and one-half inches in diameter, situated one-fourth of an inch below the surface midway between the vertex and the base, that is, in the arm area, and more particularly in the hand area.

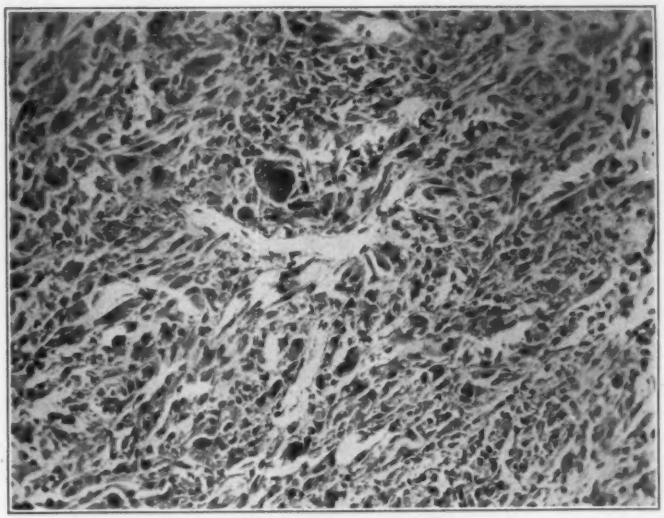

FIG. 1.—Hypernephroma.

Microscopically, the primary tumor mass, as will be seen in the photomicrographs, consisted of cells running in columns arranged about capillaries, the appearance resembling closely that of the cortex of the adrenal gland. The nuclei stain deeply, but the protoplasm stains only lightly with eosin and shows numerous vacuolations. Here and there in the strands are seen some cells much larger in size than the majority, taking a deeper eosin stain and exhibiting granular degeneration or fragmentation of their nuclei (Fig. 1).

In the metastases in the liver the general resemblance to the

adrenal cortex is retained, but is interrupted frequently by indecriminate masses of cells with no particular arrangement, and by the presence of a greater number of the larger degenerating cells (Fig. 2).

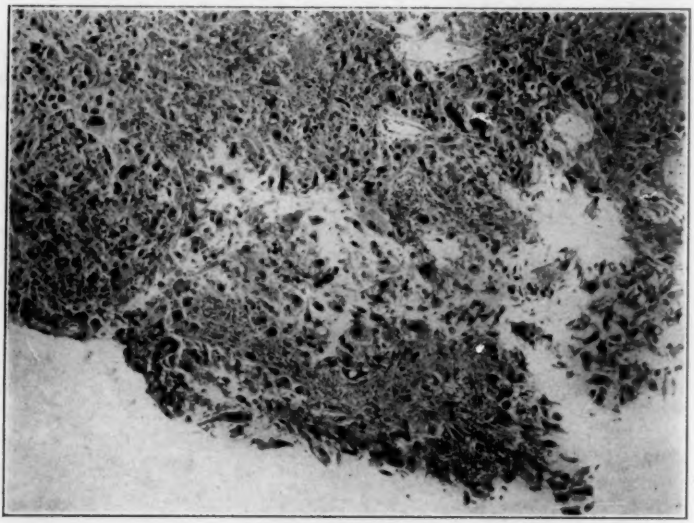

FIG. 2.—Hypernephroma. Metastases in liver.

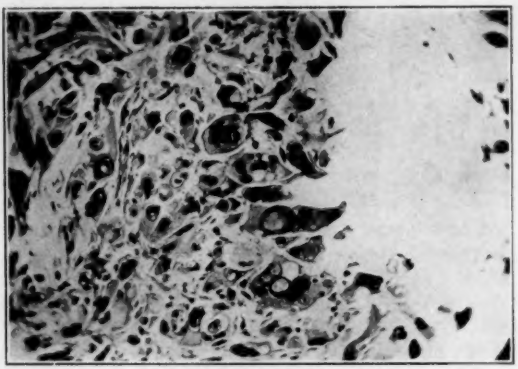

FIG. 3.—Hypernephroma. Metastases in brain.

In the metastasis in the wall of the duodenum the resemblance to adrenal tissue is maintained.

When, however, we come to look at the metastasis in the brain, all suggestion of adrenal tissue is lost. The cells are large in size,

polyhedral in shape, stain deeply, and show nuclei in many stages of degeneration. Some nuclei are small, deeply stained, and show no granulation. Others are large, pale in color, vacuolated, granular, and fragmented (Fig. 3).

Many of the cells in this metastasis have taken on a phagocytic function, and can be seen to have ingested red and white blood cells.

The presence of a tumor of this size in the abdomen, without having given rise to more definite symptoms betraying its presence, seems remarkable.

The abdominal wall was very fat, and though several routine examinations were made, no sign or symptom ever prompted more searching examination.

He had at no time any evidence of hemorrhage into the tumor, such as pain or hematuria, and the only symptom he complained of which is sometimes found with hypernephroma was a frequent aversion to food.

The blood pressure, of course, could be expected to give no information, since the tumor was entirely made up of tissue resembling the cortex of the adrenal gland, and this cortex has never been found to affect the blood pressure in any appreciable manner.

The extraordinary absence of the general symptoms of brain tumor is probably to be explained by the fact that the tumor had not caused considerable increase of intracranial pressure. It was this absence of symptoms that decided us not to submit him to exploratory craniotomy, despite the directness of the localizing sign that existed—namely, the Jacksonian convulsions. The rhythmic tremor that developed shortly before his death is of much interest. It has been generally taught that movements of this character conditioned by intracranial disease are indicated by impulses that arise from, or better said, are coördinated in the thalamus.

Without going deeply into the origin, histology, or dissemination of hypernephroma, we may perhaps say a word or two about this form of tumor. It is one of those which cannot be classed rightly with either the carcinomas or with the sarcomas, and will probably in future be put in a class by itself. It may be benign or malignant; that is, it may exist throughout life confined to its original location and cause no discomfort or menace to the patient's life; or it may be the seat of a hemorrhage, due to its friable composition, and so cause intense pain or even loss of life; or, yet again, it may take on a malignant character and strew the body with metastases.

In its simplest form, as a benign tumor, it can be best studied with regard to its origin. Histologically it consists of strands of cuboid cells arranged in long strands about capillary bloodvessels. This arrangement reminds one forcibly of the appearance of the cortex of the adrenal gland, and this similarity is enhanced by the pres-

ence in the cells of large quantities of a double light refracting fat which characterizes the cells of the cortical adrenal cells. This constituent may be found in the cells of even the most remote metastasis, though in the case which we report it has seemed to have disappeared in the brain metastasis.

In addition to this histological resemblance to the adrenal gland the location of the tumor is also most significant. Besides its occurrence in the adrenal gland itself, where normally we find small adenomas of minute size, hypernephromas occur most commonly in the upper pole of the kidney and in the right lobe of the liver on its under surface. These parts are in very close proximity in the embryo, and when we find metastasis also occurring in the ovaries and testicles, organs which take their origin in the same close proximity, though later descending to their respective sites, we can hardly doubt the origin of this tumor. This conception of hypernephromas must lead one to regard it as a congenital phenomenon. Later in life, sometimes, we see it take on an activity signifying an entire change of character. It starts to grow rapidly, to invade surrounding tissues and organs, and to disseminate metastases in many different parts of the body. The most common place to find these secondary tumors is in bone, but we here record a metastasis in the brain, in which location many statistics regarding hypernephromas record only one or two instances.

METABOLIC OBSERVATIONS ON AMYOTONIA CONGENITA.

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and
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Amyotonia congenita, or myatonia congenita, is a rare condition affecting children, aged up to three or four years, and exceptionally later, with a general proximal pseudoparalysis, for which no satisfactory etiology or pathology has been advanced. According to a recent clinical review of the subject by Haberman,[1] about 35 cases had been reported up to 1910. Since then a case has occurred in the service of Dr. J. P. Crozer Griffith at the University Hospital, Philadelphia, and was reported by him.[2] Griffith has

[1] Amer. Jour. Med. Sci., 1910, cxxxix, 383.
[2] Archiv f. Kinderheilkunde, 1910, liv, 241; Trans. Amer. Ped. Soc., 1910, xxii, 184.

collected 49 cases, including Haberman's and his own, although he admits that the diagnosis of some of them is doubtful. According to either series, however, the rarity of the disease is evident. Griffith's case, a boy, aged fifteen months, on admission, December, 1910, showed the characteristic findings of amyotonia congenita —extreme muscular weakness without signs of muscular atrophy and without evidence of rickets. The general nutrition appeared to be good. There was absence of the tendon reflexes, and entire absence of contraction both to faradic and galvanic currents.

It occurred to us that some metabolic studies in the case would be of interest. The child's condition during the first few months of his stay in the hospital precluded the possibility of making metabolic observations owing to his extreme asthenia which was increased, from time to time, by slight febrile attacks, the exact cause for which could not be determined. In June, 1911, when he was aged twenty-one months, his condition having improved, we were able, through the courtesy of Dr. Griffith, to obtain a five-day observation. The publication of our findings has been postponed until they could be controlled by similar studies upon normal children of the same age, which we have now made.

In October, 1911, the child developed an attack of bronchitis, quickly followed by pneumonia, which resulted fatally within five days. The autopsy was performed by Dr. B. S. Veeder—the results of which, together with the histological study, were published by Drs. Griffith and Spiller.[3] A summary of their important findings in the muscular and nervous system showed a brain of extraordinarily large size (as large as that of an adult), but otherwise presenting no gross anomaly. The nerve cells of the anterior lobes were scarce, and those present were much atrophied. The anterior roots throughout the cord were smaller than normal, and stained imperfectly by the Weigert-hematoxylin method. A peripheral nerve examined was found to be much degenerated. The intramuscular nerve fibers also showed degeneration. The muscular system (back, forearm, and calf) showed marked atrophy of the fibers in some places; in others the fibers were well preserved. There was an excess of fibrous and fatty connective tissue, increase in size of some muscle fibers, and fatty change within others. The muscle spindles appeared to be normal. From their study of this case and a review of others reported with autopsy, Griffith and Spiller conclude that in the lighter cases of amyotonia the pathological changes may be confined to the muscular tissues. In intense cases the nervous system is affected in a marked degree. The relations of the disease to muscular dystrophy and to the Werdnig-Hoffmann type of muscular atrophy are as yet undetermined. The points of resemblance to both these diseases cannot be ignored.

[3] Amer. Jour. Med. Sci., 1911, cxlii, 165.

There is grouped under the caption of neurology, however, a considerable variety of diseases, for whose inclusion there little or no etiological or pathological justification can be advanced. Some of these diseases to be sure, do not belong clearly in any other branch of medicine; but in any event they have been largely removed from the consideration of workers in lines outside those of neuropathology, in the broader sense of the word. In the absence of means of attack other than histological study little or no progress has been made toward their solution. Examples of this are well seen in the condition now under discussion, in the muscular dystrophies, paralysis agitans, myasthenia gravis, etc.

In certain previous communications,[4] one of the present writers has endeavored to approach some of these conditions from a different standpoint embodying a "dynamic point of view;" that is to say, a consideration of the body metabolism. The results were interesting and seemed to justify further attempts of the sort when opportunity presented. But few such studies are on record.

There seems to be no adequate reason for the indifference with which these interesting diseases have been regarded in this country by internists and laboratory men at large since the inclusion of such conditions within the realm of neurology is, largely, the result of excursions by neurologists into the field of medicine.

The phenomena of diseases such as those mentioned above are obviously of the widest importance in studying the metabolism of the muscles and of the body as a whole, as is so well exemplified in our recently acquired knowledge of tetany, for instance. But one observation seems to be on record, however, of the metabolic features in amyotonia congenita, and that one is by Spriggs, who studied the uric acid and creatinin and found a low output of the latter in a boy, aged four and one-half years (0.06 gram creatinin *per diem*).

The experiences above referred to in regard to Myasthenia gravis and Myotonia atrophica developed an interesting departure from the normal in the former disease which suggested the advisability of including a consideration of the calcium metabolism in further studies on allied conditions. The case to be reported was therefore, studied with respect to the urinary nitrogen, fecal nitrogen, urinary calcium, fecal calcium, and the creatinin. For control the metabolism of 2 normal children of the same age was also observed. All 3 children were placed upon the same diet and were kept in Bradford frames to facilitate collections. The difficulties incidental to metabolic studies upon young children are too well known to require mention here except to say that they operated to prevent our obtaining an accurate balance in the

[4] Pemberton, Amer. Jour. Med. Sci., June, 1910; ibid., February, 1911.

case of amyotonia. The essential facts sought for were elicited, however, in regard to the creatinin and fairly clearly indicated in regard to the calcium.

Although an accurate balance was impossible in the case of amyotonia, it was obtained in the 2 control cases as a further index of comparison and for possible future reference.

CASE I.—John, aged thirty-three months; normal; control case.

AVERAGE DIET.

Breakfast:	Bread	24 grams
	Butter	7 grams
	Eggs	51 grams
	Milk	100 c.c.
Dinner:	Rice	43 grams
	Butter	7 grams
	Crackers	13 grams
	Milk	100 c.c.
Supper:	Bread	36 grams
	Butter	5 grams
	Eggs	48 grams
	Milk	100 c.c.

Ingesta.

Nitrogen	12.4721 grams
Calcium	1.4604 grams

CASE II.—Alvin, aged forty months; normal; control case.

AVERAGE DIET.

Breakfast:	Bread	36 grams
	Butter	10 grams
	Eggs	54 grams
	Milk	100 c.c.
Dinner:	Rice	38 grams
	Bread	19 grams
	Butter	14 grams
	Milk	100 c.c.
Supper:	Rice	57 grams
	Crackers	13 grams
	Butter	10 grams
	Milk	100 c.c.

Ingesta.

Nitrogen	11.9805 grams
Calcium	1.4248 grams

CASE III.—Charles, aged twenty-one months; amyotonia congenita.

DIET.

	Nitrogen.	Calcium.
Bread	6.8816 grams	0.1594 grams
Rice	0.8103 grams	0.0752 grams
Egg	4.7388 grams	0.2055 grams
Butter	0.1048 grams	0.0372 grams
Crackers	0.7548 grams	0.0139 grams
Milk	16.4479 grams	3.7652 grams
	29.7382	4.2564

	Before metabolic period.	After metabolic period.	Average.	Kgs.
Weight, Case I, John	24.5 oz.	24.14 oz.	24.9 oz.	11.16
Weight, Case II, Alvin	24.4 oz.	24.8 oz.	24.6 oz.	11.07
Weight, Case III, Chas.	21.8 oz.	22.8 oz.	22.0 lbs.	10.00

CASE I.—John. April, 1912.

	7th	8th	9th	10th	11th
Quantity of urine	257 c.c.	L	320 c.c.	175 c.c.	155 c.c.
Nitrogen of urine	3.7900 grams	O	4.6592 grams	3.3712 grams	2.4416 grams
Creatinin of urine	0.1041 grams	S	0.1149 grams	0.0547 grams	0.0662 grams
Calcium of urine	Not done	T	0.1168 grams	0.0507 grams	0.0528 grams

Total nitrogen in total feces = 1.7112 grams. Total urinary nitrogen = 10.4720 grams
Total calcium in total feces = 1.7054 grams. Total urinary calcium = 0.2203 grams

Total nitrogen egested . . . . . 12.1832 grams
Total calcium egested . . . . . 1.9257 grams

Positive nitrogen balance +0.2889 grams. Weighed 24 lbs., 5 oz. before metabolic period
Negative calcium balance —0.4653 grams. Weighed 24 lbs., 14 oz. after metabolic period.
Daily creatinin average, 0.0786 grams. Creatinin coefficient, 7.04 mg.

CASE II.—Alvin. April, 1912.

	10th	11th	12th
Quantity of urine	154 c.c.	238 c.c.	298 c.c.
Nitrogen of urine	2.1905 grams	4.4382 grams	3.1752 grams
Creatinin of urine	0.0738 grams	0.1083 grams	0.0850 grams
Calcium of urine	0.1615 grams	0.2651 grams	0.1554 grams

Total nitrogen in total feces = 1.4483 grams. Total urinary nitrogen = 9.8039 grams.
Total calcium in total feces = 1.2640 grams. Total urinary calcium = 0.5829 grams.

Total nitrogen egested . . . . . 11.2522 grams
Total calcium egested . . . . . 1.8469 grams

Positive nitrogen balance . . . . . = +0.7283 grams
Negative calcium balance . . . . . = —0.4221 grams
Daily creatinin average . . . . . = 0.08903 grams
Creatinin coefficient . . . . . = 7.04 mg.

Case III.—Charles. June, 1910.

	10th	11th	12th	13th	14th
Quantity of urine	226 c.c.	168 c.c.	213 c.c.	199 c.c.	218 c.c
Nitrogen of urine	4.627 gms.	3.957 gms.[5]	3.288 gms.	3.7419 gms.	3.864 gms.[7]
Creatinin of urine	0.017 gms.	0.015 gms.	0.018 gms.	Too low to be read[6]	Too low to be read[6]
Calcium of urine	0.07677 gms.	0.02624 gms.[5]	0.0136 gms. No stool today	0.00889 gms.	0.0057 gms. 0.87192 gms. Ammonia nitrogen.

Total nitrogen of feces	2.2862 grams	Total nitrogen of urine	19.478 grams
Total calcium of feces	2.6971 grams	Total calcium of urine	0.1312 grams

Total nitrogen egested			21.7642 grams
Total calcium egested			2.8283 grams
Ingested nitrogen,	29.7382 grams	gained 1 pound	Positive nitrogen balance
Egested nitrogen	21.7642 grams		
	7.9740 grams		7.9740 grams
Ingested calcium,	4.2564 grams		Positive calcium balance.
Egested calcium,	2.8283 grams		
	1.4281 grams		1.4281 grams

Daily creatinin average	0.0166 grams
Creatinin coefficient	1.66 mg.
Daily creatinin average in Sprigg's case	0.0625 grams
Creatinin coefficient in Sprigg's case	4.0 mg.
Normal, 7 to 11 mg.	

(Creatinin coefficient = the daily creatinin elimination in milligrams of creatinin per kilo of body weight.)

A consideration of the figures reveals some points of interest. The creatinin shows a great departure in Case III (amyotonia) from both of the normal controls and even from Sprigg's case. The average daily creatinin output, when it could be estimated at all, was 0.0166, whereas in Sprigg's case it was 0.0625, and in our 2 normal cases, 0.0786 and 0.0890 respectively. This gave creatinin coefficients as follows:

Amyotonia congenita (Case III)	=0.66 m. creatinin
Amyotonia congenita (Sprigg's case)	=4.0 m. creatinin
Normal child, Case I	=7.04 m. creatinin
Normal child, Case II	=8.04 m. creatinin

[5] These figures are missing and are averaged from those preceding and following. Some urine was spilled by an attendant, leaving enough for creatinin only, though the total quantity was known from the ward record. Having all the calcium figures but those for one day, it is possible to approximate a balance, since the urinary calcium is low in any event. The nitrogen balance can be approximated in the same way, though with greater possible error.

[6] No reading possible with 10, 20, or even 40 c.c. urine. This was corroborated by Dr. Wm. Welker.

[7] On this day the nitrogen of the ammonia was approximately 22.3 per cent. of the total nitrogen.

Until we know the full meaning of the creatinin excretion, interpretation of such results must be guarded, but they would seem to be valuable, at least from the diagnostic standpoint, in differentiating amyotonia from the many conditions with which it may be confused, especially if the involvement be slight. To what extent these figures, together with Sprigg's, indicate a true disturbance of the internal muscular metabolism, is problematical but they are certainly highly suggestive.

As mentioned before, an exact calcium balance was impossible in our case, though in any event the inequalities in the excretion of calcium necessitate guarded conclusions as to its elimination, unless the metabolic period be protracted or the differences observed great. The development of fever after the last metabolic day recorded, prevented the continuation of our observations and subsequently the condition of the child, never very robust, precluded a repetition of the experiment. So far as our figures go, however, and the general facts seem fairly clearly indicated, there is no evidence of marked disturbance in the calcium metabolism.

In observations on a case of myasthenia, previously mentioned, a decided calcium loss was noted over a metabolic period of a week, and it was thought that the present case might show some analogy to it; the opposite is suggested, however.

In conclusion, obligation should be expressed to the Board of Managers of the Presbyterian Hospital, Philadelphia, for the installation of the facilities which have made this and other studies possible. Acknowledgment is also due Dr. Damon B. Pfeiffer, director of the pathological laboratory, for his courteous coöperation on many occasions.

REVIEWS

A Manual of Surgical Treatment. By Sir W. Watson Cheyne Bart., C.B., D. Sc., LL.D., F.R.C.S., F.R.S., Hon. Surgeon in Ordinary to H. M. the King, Senior Surgeon to King's College Hospital; and F. F. Burghard, M.S. (Lond.), F.R.C.S., Surgeon to King's College Hospital, and Senior Surgeon to The Children's Hospital, Paddington Green. New edition entirely revised and largely rewritten with the assistance of T. P. Legg, M.S. (Lond.), F.R.C.S., Surgeon to the Royal Free Hospital; and Arthur Edmunds, M.S. (Lond.), F.R.C.S., Surgeon to the Great Northern Central Hospital, and Surgeon to Out-Patients, The Children's Hospital, Paddington Green. In five volumes. Vol. I, pp. 552; 223 illustrations. Vol. II, pp. 570; 252 illustrations. Philadelphia and New York: Lea and Febiger, 1912.

The first edition of this Manual of Surgical Treatment comprised seven volumes and was published from 1899 to 1903. The present edition is being issued in five volumes. The work has been entirely revised and largely rewritten; for this purpose the authors have invoked the assistance of Messrs. Legg and Edmunds, because, as the preface informs us, "the pressure of other work rendered it impossible for the original authors to undertake a task of such magnitude with any hope of being able to complete it within a reasonable time." The authors have also enlisted the advice and assistance of Dr. Silk, Dr. D'Este Emery, Dr. Arthur Whitfield, and Mr. A. D. Reid, who have supplied material for the sections dealing with such special subjects as anesthetics, blood examinations, preparation and use of vaccines, etc.

The design of the work is to afford the reader clear and practical advice on the treatment of all conditions in surgery. Pathology and diagnosis are not entirely ignored, but are discussed only when absolutely necessary to explain the treatment advocated. The methods of treatment recommended are such as have proved acceptable to the authors, and in very few instances is it apparent that they have not been employed and tested personally. These features are those which constitute the work a Manual in the intellectual sense. There are few references of historical or bibliographical interest; contemporaneous writers seldom are quoted by name, even if their practices are adopted; and the teaching

inculcated rests in almost all instances on the unsupported *ipse dixit* of the distinguished authors. This is as it should be for a work of this kind, which is neither a text-book, a monograph, nor an encyclopædia. It is a Manual. And in the true original sense of the word the work is a manual also. Each volume is handy in size, in spite of the fact that each contains much more matter than one volume of the previous editions. It is a work for constant use.

In the first volume what is now popularly spoken of as general surgery, and which formerly was described as the principles or the institutes of surgery, is discussed in some three hundred pages; the subject of deformities is also included (about 150 pages); and an appendix is added in which Dr. Silk discusses anesthetics, and Dr. Emery describes in rather summary fashion methods of blood examination, the preparation and use of vaccines, etc.

Of course, going through the chapters page by page, much is found worthy of comment. Not all of these points can be discussed here. A few omissions may be noted: No mention of position in the control of hemorrhage; nothing about continuous baths in the treatment of burns; nothing about carbolic acid injections in tetanus, and the advice, which we regard as a fault of commission, to administer intracerebral injections of antitoxin in this disease. Direct transfusion of blood is ignored. The spelling "Scepticæmia," which occurs repeatedly in the table of contents, should not have escaped the proof-reader's eye.

Antisepsis still is preferred to asepsis, and the chapters on wound treatment are one of the portions of the work which seem in the opinion of the authors to have required least revision.

The statement that the decision for or against a mutilating operation for malignant growth should be left to the patient, is one that brings up anew the moral duty of surgeons. No doubt in all cases the ultimate decision for or against operation rests and must rest with the patient or his friends, for the tumor belongs to the patient and not to the surgeon. But surely the surgeon should not be regarded, much less should he regard himself as a mere machine, to do the cutting if the patient so decides, or to stand by in idleness if the patient declines. We believe the surgeon in such cases should be more than a passive onlooker. Every patient knows that after a serious operation he may die or he may get well, and that the degree of mutilation may be extreme if he survives. But what he looks to the surgeon for in his dire extremity is not a statement of the percentage mortality of the proposed operation, but the expression of a sincere conviction that in this individual case the operation is or is not advisable. This is what a good surgeon can tell far better than even the most intelligent patient; and when even the most timorsome patient feels that the surgeon stands between him and grim fate in such an attitude as

this, there are very few instances in which this throwing the entire responsibility on the surgeon is not a consolation to the patient and all his anxious family. Hence we believe the statement of the authors, that the surgeon should content himself with placing the facts fully before the patient, is an error.

The chapters on deformities are scarcely equal to other portions of the book. Nearly seven pages are devoted to so simple a thing as tenotomy of the tendo Achillis and the after-treatment, and much of this is quite unnecessary twaddle. The treatment of congenital dislocation of the hips and of scoliosis is such as was employed nearly ten years ago; these sections should be entirely rewritten.

Dr. Silk, in his discussion of anesthetics, shows the usual modern tendency away from the use of chloroform.

Dr. Emery says of the von Pirquet test for diagnosis, that it is "almost absolutely trustworthy in children up to the age of twelve or fourteen years;" of the subcutaneous test, for older patients, he gives 0.001 gram first, and if no reaction occurs, goes at once to 0.003 or 0.004 gram. Treatment with tuberculin he considers only a *pis aller;* it is difficult to cure by it lesions in which there is a large amount of caseous material or much fibrosis; "good results," he adds, "are occasionally obtained with tuberculous glands, but this is the exception, and as a rule it is better to remove them."

The second volume includes treatment of lesions of the skin and subcutaneous tissues, nails, lymphatic vessels, and glands, fasciæ, bursæ, muscles, tendons and their sheaths, nerves, veins, arteries and aneurysms; as well as bones, in which latter section are comprised fractures, bone diseases, rickets, and tumors of bone. The volume closes with two chapters on amputations.

Expert advice has been enlisted from Dr. Whitfield on the treatment of lupus, and from Mr. Reid on the treatment of rodent ulcer by radium and the *x*-rays.

The authors strangely cling to the fearsomeness of pre-antiseptic days in their timidity about opening a chancroidal bubo. Modern surgery has demonstrated that secondary infection is the only thing to be feared; and pathologists seem to believe that the bacillus of Ducrey is self-destroyed by the pus which it produces.

As regards the treatment of aneurysms, the authors show, with continental surgeons, a preference for extirpation of the sac over the method of Matas. This they damn with faint praise as follows: "We have given the full details of this operation because it has been done already with a fair amount of success in a considerable number of cases, especially in America. It must be, however, difficult to perform successfully, and it is probable that further experience will show it to be only of limited applicability." Many new illustrations have been introduced in the chapters on ligations,

and in most other respects these sections have been brought fully up to date; there is no mention, however, of the posterior route for ligation of the first part of the left subclavian artery.

Fractures are considered at great length, nearly 200 pages. The authors favor the administration of a general anesthetic for reduction in almost all cases; they favor operation "as soon as possible" when it is called for, and they think it is called for rather frequently. They do not except from this rule children, in whom it is well known that even wide separation of fragments may give no disability or shortening if alignment is preserved; and they do not recognize that oblique require less accurate reduction than transverse fractures. There is no mention of nail extension after the methods of Codivilla and Steinmann, nor the use of a compound pulley for reduction, or of the possibility of reduction by angulation. They approve massage and mobilization in moderation. In cases of compound fractures they urge extensive operation with plating or use of wire fixation.

Volkmann's contracture is discussed as a complication of fractures; but strangely there is no mention whatever of Jones's very efficient orthopedic treatment of this condition. Apart from operation they mention only massage and passive movements under the heading of non-operative treatment.

Their practise of beginning passive movement in the case of elbow fractures at the end of a fortnight and their insistence that *full* extension, flexion, supination, and pronation must be enforced once daily from that time on, explain their further statements that not only do adhesions occur in the joint, but a considerable mass of callus is thrown out, etc. If, after accurately reducing the fracture, and keeping it reduced for about three weeks, they would then leave the child's elbow alone, they would be surprised to find that recovery of full function would occur without any callus or the necessity for any passive movements.

The sections on osteomyelitis are not up to date; thorough scraping out of the medulla in acute cases is still recommended, though it was shown by Nichols, a number of years ago, to be not only unnecessary but harmful. The paragraphs on bone transplantation read like ancient history, since the recent work in this line of J. B. Murphy, but as the present volume antedates the publication of these remarkable successes, the authors are not to blame.

Little change is apparent in the chapters on amputations; though the authors bravely commence the subject by pointing out the greater deliberation of present-day operating and the increasing favor of irregular flaps, they at once revert to the description of stereotyped forms. Nor is this to be condemned, because the types must first be learned, and learned well, before a surgeon can successfully introduce variations of his own. But surely in a

work of this size there should be space for a description of Bunge's aperiosteal method for the purpose of securing end-bearing stumps, as well as some mention of amputations for cinematic prosthesis.

The volumes, as already noted, are of convenient size; the paper is good; the type is clear and of fair size; and very many new illustrations (mostly half-tones) have been added, the old ones being discarded where something better was available. There is, however, a tendency toward repeating the same illustration an unnecessary number of times. But the work fulfils its purpose, and will be heartily welcomed by the profession. A. P. C. A.

PELLAGRA, AN AMERICAN PROBLEM. By GEORGE M. NILES, M.D., Professor of Gastro-enterology and Therapeutics, Atlanta School of Medicine. Pp. 253. Illustrated. Philadelphia and London: W. B. Saunders Co., 1912.

PELLAGRA has been under observation and study in European countries for nearly two centuries, and yet little accurate knowledge exists as to its etiology, transmission, or treatment. It has at last come into our own country and is presenting its problems to us in a very definite form. The scourge, for such it promises to be unless active measures are at once instituted to check it, is so frightful and awful in its results that any work or observation which promises to clear up its mysteries should be gladly welcomed. In the present work Niles has done us a great service in presenting in brief form the present ideas of pellagra as culled from the writings of many observers abroad and in this country, as well as from his own rather large experience in the study and handling of this disease.

The work is divided into ten chapters. The historical sketch and the chapter on etiology are particularly interesting, and bring out strongly the relationship between pellagra and spoiled maize. And although this etiological relationship is not generally accepted, the author feels that he is justified in closing the chapter on etiology with a reiteration of Lombroso's theory that "In pellegra we are dealing with an intoxication produced by poisons developed in spoiled corn through the action of certain microörganisms in themselves harmless to man."

The chapter on symptomatology and course is well systematized and frequently interspersed with clinical illustrations and case reports to show the many and varied manifestations of the disease.

The chapters on treatment and prophylaxis cover well the present ideas on these subjects, but they must both be necessarily a little vague until the question of etiology is definitely settled.

An interesting and instructive portion of the book is the chapter on animal experimentation and deductions in which the author brings his work up to the knowledge of the day from the experimental side.

There seems to be no great advance in our knowledge of the disease described nor any radical or new ideas expressed, but the work stands as a very complete *resume* of the best and most recent conceptions of the disease, and a starting point for the advance work of the future which must come before complete solution of this "American problem" can be reached. The book is well put together, is very readable, well printed, and the illustrations are unusually good. F. H. K.

CLINICAL DISORDERS OF THE HEART BEAT. By THOMAS LEWIS, M.D., D.Sc., M.R.C.P., Lecturer in Cardiac Pathology, University College Hospital Medical School. Pp. 104, 48 diagrams. London: Shaw and Sons; New York: Paul B. Hoeber, 1912.

THERE are few who are not aware of the great strides that have been made in recent years regarding our knowledge of the mechanism of the heart beat and its disorders, by means of precise graphic methods. Because of the difficulty of applying these methods without special training and study, disorders of the heart beat have not received from the majority of medical men the attention that their importance merits. Many are still content to speak of a pulse rhythm in vague terms such as "very irregular" or "somewhat irregular" or "intermittent" or "bigeminal," without attempting to identify these disturbances exactly, as they can and should be.

It has long been noted that only in certain cardiac cases, digitalis preparations have been efficient in lowering the pulse rate and improving the patient's condition. Where it has not been efficient, the preparation has been blamed and another form used, or one of the other remedies with more or less reputation as a cardiac "stimulant" has been substituted. We know now, thanks mainly to the careful observations of James Mackenzie, that the nature of the disturbance determines the efficacy of the drug; that the totally irregular pulse of auricular fibrillation is *par excellence* the condition responding most frequently to medication by drugs of the digitalis group; that hearts with normal rhythm respond in not more than 30 per cent. of cases; and that various other types of irregularity either do not call for the drug or even contraindicate its use. It, therefore, behooves the medical attendant to recognize very clearly beforehand what the results of his medication are

likely to be. This he can do by simple means without graphic records; and it is to help in such recognition that Lewis has written this hand-book. How well he has done it, any one acquainted with his previous writings and his numerous contributions to the field of cardiac research will know.

The book comprises seven chapters on sinus irregularities, heart-block, premature contractions (extrasystoles), paroxysmal tachycardia, auricular fibrillation, and pulse alternation. In each instance, the nature of the disturbance, its etiological and pathological relations, its subjective symptoms, recognition, prognosis, and treatment are described. Most cases of pulse alternation can scarcely be recognized without graphic means, and here Lewis recommends the use of a simple instrument, such as the Dudgeon sphygmograph. The arrangement of the book is methodical, and its style as clear and concise as the book itself is brief. Lewis aims to bring to general recognition essential facts that have hitherto been known to comparatively few. His book is a valuable contribution, and deserves to be widely read. H. G. S.

DELAYED AND COMPLICATED LABOR. By ROBERT JARDINE, Professor of Midwifery in St. Mungo's College, Glasgow. Pp. 343; 107 illustrations, 3 in colors. New York: William Wood & Co., 1912.

THIS book is evidently designed, on the principle of clinical lectures, for ready reference and to assist in a rapid decision as to plan of treatment in all the emergencies likely to be met in obstetric practice. As such it will prove useful. Many points about it are exceedingly good, notably the chapters on hemorrhage; the routine and operative treatment of eclampsia; the chapter on forceps operations and embryotomy, and especially the pages (Chapter X) on Baudl's contraction ring. This latter subject is fully and ably treated, whereas in many similar books it is passed over in a most superficial manner, although it would be difficult to imagine a complication that would get a man of moderate experience into into deeper water in so short a time as a case of retraction ring improperly managed. The author states that this is a "one man book," and that he hopes it will be so considered. There are many points, of course, where the technique described is open to discussion and perfectly justifiable difference of opinion, but there can hardly be two opinions as to the aseptic technique, which is distinctly bad. Rubber gloves, universally, do not seem to be known in Glasgow, and hardly an illustration of technique but shows bare hands and arms. Again, many of the illustrations are

not good, especially for the use of medical students, for whom clearness is an absolute essential. Again, the almost veterinary Champêtier bag will not reap much favor here, where it has been almost discarded. There is no mention of blood pressure in the otherwise excellent article on eclampsia; or of Brunn's extraperitoneal Cesarean section, at least as important an operation as the Porro. In future editions, the chapter on pelvic deformities could be improved, for use in this country, by the inclusion of measurements in centimeters as well as inches.

The arrangement of the book is good, however, with the headings in heavy type and well adapted to quickly finding the information sought, and the work should prove of value in the field it covers.

J. C. H.

SURGERY OF DEFORMITIES OF THE FACE, INCLUDING CLEFT PALATE. By JOHN B. ROBERTS, A.M., M.D., Professor of Surgery in the Philadelphia Polyclinic; Surgeon to the Methodist Hospital, Philadelphia, etc. Pp. 273; 273 illustrations. New York: William Wood and Co., 1912.

THIS work gives a detailed account of the congenital and acquired deformities of the face, with their correction by surgical means, profusely illustrated with cases from the wide personal experience of the author. His special leaning to plastic surgery has made him an authority on the subject.

The chapters on hare-lip and cleft palate are probably the most important in the book, and are unsurpassed for clearness in the description of methods of treatment. The author shares the opinion of Lane and Brophy that congenital cleft palate should be closed as early in life as possible, and that it should be operated upon first in cases combined with hare-lip. The operative methods of Lane are especially advocated for cleft palate, and are fully described and illustrated.

There is a useful chapter on skin diseases requiring surgical treatment. Three modern methods of treatment of skin lesions are not described, viz., vaccine therapy in acne vulgaris, desiccation of small growths such as warts, moles, and epitheliomas, with the high frequency current, and the employment of carbon dioxide snow for the obliteration of nevi and other growths. As these procedures have all met with recognized success, it is to be regretted that they are not at least mentioned.

Dr. Roberts' views on the treatment of hypertrophied tonsils do not agree with those of laryngologists at the present time. In advocating removal only of the portion of the organ projecting into the fauces, he apparently overlooks the fact that it is the

"buried" variety—which does not project at all—that is most frequently diseased, and therefore requires complete extirpation.

The author probably recognizes as well as anyone the difficulty of making complete a regional work of this kind without infringing on the fields of specialists in ophthalmic and rhinologic surgery. No doubt this is the reason he has described at length such conditions as ectropion, ptosis, symblepharon, etc.

The text is profusely illustrated with excellent cuts, most of them original. Fig. 95, taken from Bryant and Buck's "Surgery," does not show the correct anatomical relation of the tongue and palate with the mouth closed. The dorsum of the tongue should be in close contact with the roof of the mouth and soft palate, and the space between it and the post-pharyngeal wall should be much narrower. There are a few typographical errors of minor importance.

Frequent references to the literature, clearness of expression, and attention to detail, combine to render the book the most complete and useful of modern works on the subject. R. H. I.

DIE STÖRUNGEN DES FARBENSINNES IHRE KLINISCHE BEDEUTUNG UND IHRE DIAGNOSE. Von DR. HANS KÖLLNER, Privatdozent an der Universität Berlin, Assistent der Universitäts-Augenklinik. Pp. 415; 33 illustrations and 3 colored plates. Berlin: S. Karger, 1912.

HERE is a book of 415 solidly printed octavo pages devoted exclusively to disturbances of the color sense. A work of this size upon such a limited subject allows of ample opportunity for a thorough exposition and discussion of every factor, theoretical and practical, which can enter into the subject matter. Indeed, while the author and the profession are both to be congratulated upon the former having brought together about all that relates to the matter in hand, the reader may entertain the thought that there is almost too much and that condensation would have spared him some hours of rather weary labor; for the book is by no means easy reading, partly owing to the nature of the subject which trenches upon psychology, physiology, and physics, with all of which sciences the reader should have some acquaintance. Following a short discussion of the normal color sense, which is the one portion of the subject we might wish that the author had treated somewhat more *in extenso*, the congenital anomalies (monochromatism and dichromatism) and incompleteness of normal trichromatism are taken up.

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HERE is a book of 415 solidly printed octavo pages devoted exclusively to disturbances of the color sense. A work of this size upon such a limited subject allows of ample opportunity for a thorough exposition and discussion of every factor, theoretical and practical, which can enter into the subject matter. Indeed, while the author and the profession are both to be congratulated upon the former having brought together about all that relates to the matter in hand, the reader may entertain the thought that there is almost too much and that condensation would have spared him some hours of rather weary labor; for the book is by no means easy reading, partly owing to the nature of the subject which trenches upon psychology, physiology, and physics, with all of which sciences the reader should have some acquaintance. Following a short discussion of the normal color sense, which is the one portion of the subject we might wish that the author had treated somewhat more *in extenso*, the congenital anomalies (monochromatism and dichromatism) and incompleteness of normal trichromatism are taken up.

Among the callings unfavorably influenced by defect of the color

sense, railway and marine service, art, the author gives a place to that of the practicing physician; defects in whose color sense will interfere with the ready recognition of certain exanthemata of the skin and mucous membrane, commencing icterus, color changes in the eye ground, etc., as well as certain appearance in chemical tests and microscopic diagnoses, for example, the methyl-violet test for gastric juice, staining effects upon bacteria, etc.

Of acquired disturbances of the color sense, which occupy the remaining three-quarters of the work, the various forms are discussed *seriatim*, blue-yellow blindness, progressive red blindness, total color blindness together with the various forms of chromatopsia and cortical disturbances. Pathological changes in the dioptric apparatus, diseases of the retina and choroid, and of the optic nerves and tracts are considered in detail as affecting the color sense. The neuroses, hysteria, neurasthenia, etc., are given a chapter to themselves.

The average reader whose acquaintance with disturbances of the color sense has been derived from the meagre accounts with which even the best of the text-books content themselves, will experience surprise at the extent of the subject and its numerous subdivisions. The simple tests with the Holmgren yarns and the usual methods of investigating the color sense in railway employees are very elementary and fail in many changes to uncover important defects, to say nothing of establishing an exact diagnosis. The careful investigations which have been made in the last decennial have had to be sought for in the periodical literature where they have been widely scattered and often inaccessible. This is the first attempt to bring the results together in a single volume.

T. B. S.

DISEASES OF INFANTS AND CHILDREN. By HENRY KNIGHT CHAPIN, Professor of Diseases of Children, New York Post-Graduate School and Hospital, and GODFREY ROGER PISEK, Professor of Diseases of Children, University of Vermont. Second edition; pp. 617; 181 illustrations and 11 colored plates. New York: William Wood & Co..

THE second edition of this book appears with but slight changes in the text. The additions are such as would be expected, and include virtually all the recent advances in medical sciences pertaining to pediatrics. The authors have only added 27 pages and 2 illustrations to the new edition, thus preserving the compact and convenient size of the volume. The chapter on special examinations might well have been entirely omitted, or at least considerably abbreviated. This applies particularly to the paragraphs

on the Wassermann test, dealing with the theory of the reaction. This space, some 6 pages, could have been more advantageously employed in elaborating throughout the book the too brief pathology of the various diseases rather than going into an elaborate discussion of a subject more or less foreign to a work of this kind. In the same way the various tuberculin reactions, the Widal test, and such diagnostic methods might better have been abbreviated and then incorporated under the specific diseases with which they are associated.

The chapters on infant feeding and the acute exanthemata are particularly valuable. The author handles the subject of infant feeding in a simple and elementary manner which is of great advantage not only to the medical student for whom the work is particularly intended, but also to those other readers of pediatric text-books, the young mothers. The subject is dealt with from a physiological standpoint, and the reader thus obtains a clear conception of infant feeding before advancing to the more intricate problems of the subject. The authors favor the top milk method of modifying cow's milk, the most convenient and satisfactory method yet devised for properly modifying the milk.

The exanthemata are taken up carefully and the rashes described fully and in detail. The value of this chapter is much enhanced by the addition of five colored plates illustrating the various rashes, thus firmly fixing upon the student's mind the general chatacteristics of these rashes in a way impossible by a mere detailed description of conditions which must be seen to be remembered.

The chapters on the commoner surgical diseases, the commoner diseases of the eye and the ear, and the diseases of the skin, while necessarily brief, are particularly of value not only to the student, but to the general practitioner, who is often at a loss to know where to turn for advice about the diagnosis and treatment of these conditions in children.

This edition preserves the same satisfactory typography and illustrations as are found in the first edition. With the careful changes and additions that have been made, the authors can safely be assured that this new edition will receive the same satisfactory welcome by students and practitioners as the earlier volume.

J. H. M., Jr.

Preventable Cancer. By Rollo Russell. Pp. 164. London: Longmans, Green & Co., 1912.

The gropings for the cause of cancer have led in many directions. In this book statistics have been industriously compiled and arguments advanced in support of the thesis that cancer is a

disease that is due largely if not chiefly to faulty habits of eating and drinking that come in the wake of civilization. Reduced to its simplest terms the argument is as follows: Cancer is due to some form of irritation as is seen in "pipe" and "chimney-sweep" cancer. The races and communities which are most scourged by cancer are those that eat and consume stimulating drinks to excess. Therefore, it is probable that these indiscreet habits are the irritant factors at the bottom of the prevalence of cancer. There is much in the book to interest the student of cancer, but after perusal the reader will probably agree that the inductive hazard is too great to compel agreement with the author's convictions. D. B. P.

Gonococcus Infections. By Major C. E. Pollock and Major L. W. Harrison. Pp. 218. London: Oxford University Press, 1912.

For student and practitioner for whom this book is designed, it may be recommended as a clear and altogether excellent summary of our knowledge of gonococcus infections. The treatment in its concise and practical detail bears evidence to the experience of the authors and possesses the advantage of not being encumbered by a multiplicity of recommendations drawn from the literature. Vaccines are highly recommended in the treatment of the metastatic infections. D. B. P.

Aids to Histology. By Alexander Goodall, Lecturer on Physiology, School of Medicine of the Royal Colleges, Edinburgh. Pp. 135; 20 illustrations. New York: Wm. Wood & Co., 1912.

This is an attempt to present the essential facts of histology in a simple manner, and in small compass for the junior student. The author has a direct, succinct style and makes the most of the short space he has allowed himself. The list of organs considered is complete, and in general the statements are trustworthy, although all may not agree with his description of cardiac muscle. It is often obvious that the clearness of the descriptions suffers from too much condensation. W. H. F. A.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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On the Causation of Parenchymatous Nephritis.—GEORGE W. WATSON (*Brit. Med. Jour.*, 1912, i, 822) reports that beyond the association of acute nephritis with the acute fevers, little is known regarding its etiology. Our knowledge is even more vague in regard to the causation of chronic nephritis. To obtain some further insight into the etiology of renal inflammations, Watson has analyzed 100 cases of nephritis in the wards of the General Infirmary at Leeds, excluding cases of interstitial nephritis, or primary sclerotic kidney occurring beyond the middle period of life. Of this series, 80 were undoubted chronic kidneys of either the "large white," or "small white indurated" type. Watson has considered these together as chronic parenchymatous nephritis. It appears that the period of life in which the onset of symptoms is commonest is between twenty and thirty. Acute infections have little or nothing to do with the production of the disease. The effect of long continued sepsis is not clear. Several patients gave a history of uniform good health except for frequently recurring "sore throats." It is therefore not unlikely that absorption of products from organisms may occur without indication of infection. Chronic lead intoxication is well recognized as a potent factor. In only 3 of Watson's cases was it possibly significant. There is no evidence that alcohol was of importance. The only definite effect appeared to be the determination of symptoms in an already existing nephritis. Watson believes that none of the factors enumerated act more than as contributing causes, and that symptoms in an adult whether suggesting an acute or chronic nephritis indicate in the majority of cases a chronic renal change. Of the fundamental cause practically nothing is known. Watson has

considered in this analysis as genuine acute nephritis, those cases in which albumin and casts disappeared permanently with the symptoms after a short time. There were 18 such with diagnosis confirmed in one. All but 2 occurred under thirty, bearing out the commonly accepted view of age incidence. There was no single convincing instance of primary acute nephritis arising from cold. Watson regards this rather as a factor producing the onset of symptoms in an already existing chronic disease, contributing by depressing the general health, and thus favoring the operation of the true cause. On the whole, Watson thinks that acute nephritis is not a common disease, and is usually due to the direct effect of some infection. The majority of cases recover completely. The diagnosis can seldom be made with certainty during the acute attack, and therefore prognosis cannot be safely given, until after at least a few weeks' interval.

On the Function of the Circle of Willis.—S. P. KRAMER (*Jour. Exper. Med.*, 1912, xv, 348) reports that in 1664 Dr. Thomas Willis published "Cerebri Anatome." Since then it has been generally believed that the circle of Willis was a kind of reservoir from which the different parts of the brain drew their blood supply. Kramer experimented with 50 live dogs and 3 monkeys in the following way. The animals were anesthetized and injected in a carotid or vertebral artery with a solution of methylene blue. The circulation was not interfered with. The animals were killed by opening the heart two minutes later. The brain and cord were removed and the distribution of dye noted. The results obtained by this method showed constant results. Kramer found that a carotid injection distributed methylene blue to the areas supplied by the anterior and middle cerebral, anterior choroid, and posterior communicating arteries on the same side. If a vertebral artery was injected with the others unobstructed, the stain went to the areas supplied by both vertebral arteries, the basilar, and both posterior cerebrals and their branches. If one vertebral artery was tied and the other injected, the staining was incomplete on the tied side. If one carotid was tied and the other injected, the parts were stained normally. But if both carotids or both vertebrals were tied, and one of the other vessels injected, the separation of areas disappeared and the stain was carried forward or backward as the case might be. In other words, the circle of Willis is an antero-posterior anastomosis between the carotid and vertebral vessels, which under physiological conditions does not permit the mingling of blood streams. When, however, either the anterior or posterior branches are completely blocked, the anastomosis will supply blood. These observations were controlled pharmacologically by injecting into the vertebral artery "bulbar poisons" which ought to produce on the centres in the medulla results which they would not cause if injected into the carotid. Alcohol, ether, and chloroform were used, both alone and in defibrinated blood from the same animal to rule out the possibility of emboli. Blood pressure and respiration were recorded. The results obtained entirely confirmed Kramer's previous observations.

Experimental Studies on the Administration of Salvarsan by Mouth to Animals and Man.—To determine the primary effects of salvarsan by mouth, JOHN A. KOLMER and JAY FRANK SCHAMBERG (*Jour. Exper.*

Med., 1912, xv, 498) administered it to a series of cats, rabbits, and dogs, in pills, capsules, or dissolved in milk and water. Results showed that the drug was without immediate toxic effects, when given in this way, to animals, in a relatively large single, or in multiple smaller doses. No late or secondary poisonous effects attributable to arsenic were seen. In doses equivalent to those used in man, no appreciable degenerative changes were found in the principal organs, within ninety-six hours. Kolmer and Schamberg consider the question of absorption of salvarsan from the intestines worthy of further study. Experiments were made with gastric contents, feces, bile, and urine which demonstrated that within twenty-four hours of ingestion of salvarsan, arsenic may be found in both bile and urine. It is probable that only a portion is absorbed, and this quickly eliminated. When the drug is given, by the mouth to cats, the number of bacteria in the intestinal tract appears to be reduced, most strikingly in the lower end of the ileum. Finally, salvarsan was given by mouth in capsules containing 0.100 to 0.600 grams to 7 syphilitic patients. One within four weeks received 2.4 grams without toxic effect. No symptoms of arsenical poisoning were encountered, unless vomiting and diarrhea, which did not occur in all cases, be considered such. Thus given, the drug exerted a therapeutic influence, but too feeble, Kolmer and Schamberg believe, to warrant its use by this route.

"Floating" or Movable Kidney Considered from the Practitioner's Standpoint.—Sir Maurice Abbot Anderson (*Practitioner*, 1912, lxxxviii, 625) believes that the two chief causes which give rise to symptoms from a movable kidney are the associated sagging of other organs, and the liability of a freely movable kidney to permit the ureter to become bent on itself. Thus symptoms are referred to the nervous system, reflexly, and the digestive or genito-urinary systems. Very often the condition may exist without any trouble save a dragging pain in the side, and tenderness of the kidney when found and manipulated. The nervous and digestive symptoms result, as a rule, from "dropped stomach" producing intolerant dyspepsia. Such cases, Abbot Anderson asserts, invariably get well provided means are taken to rectify the kidney displacement, to prevent its recurrence, and to treat the gastric condition. This may be well done by massage vibrators, which are infinitely superior to hand massage. The genito-urinary symptoms may be referable to the kidney or bladder. Among the former may be hydronephrosis or hemorrhage. Among the latter may be frequency of urination, or even swelling of the vulva associated with a certain degree of fever. Abbot Anderson has never seen a case of the first, but cites cases of the last two. Some patients get well by rest and feeding. Otherwise the treatment, Abbot Anderson thinks, should be directly surgical, or mechanical by suitable trusses or pads.

Tests of the Efficiency of Pasteurization of Milk under Practical Conditions.—Edwin Henry Schorer and M. J. Rosenau (*Jour. Med. Research*, 1912, xxvi, 127) report that the thermal death points of patholgenic organisms which sometimes invade milk, have been determined in many laboratories. It has been an open question whether

such results could be translated with safety to the pasteurization of large volumes of milk under commercial conditions. Schorer and Rosenau undertook to determine the effectiveness of commerical pasteurization. Tests were made at a large dairy, in which the method used was the "holding," consisting briefly in heating the milk to 140° to 155° F., and putting it into a receptacle which keeps the milk at this temperature from twenty minutes to an hour. Schorer and Rosenau made 4 tests with 100 gallons of milk. In two, it was planned to heat the milk to 140° F., and in two to 145° F. The temperature attempted was not attained. They tested the efficiency of the apparatus in destroying microörganisms which are most common and serious. In 2 tests with diphtheria, 1 succeeded, 1 failed; in 2 with typhoid, 1 succeeded, 1 failed; in 2 with human tuberculosis, both failed; and in 2 with bovine tuberculosis, 1 succeeded, 1 failed. However, in these cases which failed to kill the tubercle bacillus, only some of the bacteria survived. Fewer guinea-pigs inoculated with the heated milk developed the disease than control animals. The disease was more localized and atypical. From their observations Schorer and Rosenau believe that organisms in milk will be destroyed if heated for twenty minutes at 140° F. Since in practice, milk may not reach even minimum requirements, a liberal factor of safety is necessary commerically. Moreover, the process must not be unduly hurried, thus increasing the physical difficulties of heating all portions uniformly. Finally, Schorer and Rosenau consider official control of pasteurization necessary. It is as important to standardize and guard devices for the temperature recordance of a pasteurization apparatus, as to watch weights and measures.

A New Symptom of Aneurysm of the Aorta.—R. V. Hoesslin (*Münch. med. Woch.*, 1912, lix, 24) describes a type of respiration in a patient with aneurysm of the aorta, which is unique, so far as he can discover. The patient was suffering from a gradually increasing compression of the left bronchus. With the growth of the aneurysm the trachea became involved in the pressure. For two days preceding death, the inspiration was stridorous and somewhat prolonged, the expiration interrupted. It was found that the interruptions were synchronous with diastole. The phenomenon is somewhat analogous to interrupted vesicular breathing, In the latter, however, the interruptions are synchronous with systole and occur during inspiration. The cause of the "diastolic expiration," as V. Hoesslin designates the condition, is clear. The compression of the trachea had progressed to such an extent that air could escape from the lungs only during diastole, when the sac diminished in size.

Rontgen Examination and Glycyl-tryptophan in the Diagnosis of Cancer of the Stomach.—C. Kayser (*Deutsch. med. Woch.*, 1912, xxxviii, 551) finds that the interpretation of the glycyl-tryptophan test of Neubauer and Fischer is facilitated by röntgenologic studies of the stomach. From a study of 50 gastric cases, he arrived at the following conclusions: (1) The diagnosis of gastric carcinoma is simplified both by Röntgen ray examination and by the glycyl-tryptophan test of Neubauer and Fischer. Cases of cancer have been recognized by these means which

would otherwise have been missed because of the anatomical position of the tumor. (2) All cases, in which Röntgen examination and the tryptophan reaction were positive, were advanced cases of cancer. Whether the two procedures make possible an early diagnosis remains to be seen. (3) A positive tryptophan reaction makes carcinoma highly probable though a negative test does not exclude malignant disease. (4) Where the suspicion of carcincoma is strong clinically and the test is negative, it is necessary to repeat the test a number of times to avoid confusion, for the tumor may at times secrete insufficient ferment to yield a positive reaction.

A simple Method for the Determination of Uric Acid in the Blood and in other Colloidal Fluids.—F. GUDGENT and E. APOLANT (*Deutsch. med. Woch.*, 1912, xxxviii, 603) have devised a simple method for the determination of uric acid in blood and other colloidal fluids. It has been shown by Gudgent that uric acid exists in the blood only as monosodium urate, a salt which is dialyzable. By experiment he has demonstrated that none of the uric acid is in combination with protein. The authors' method is carried out by dialysis. They find that it can be performed with only 20 c.c. of blood and that the duration of the dialysis need not exceed three hours. (The simple apparatus which is required may be obtained from A. Eberhardt, Berlin, Platz vor dem neuen Tor Ia). *Method.*: After the patient has been on a purin free diet two to three days, at least 20 c.c. of blood is withdrawn from a vein. Coagulation is prevented by the addition of a small knife-point of sodium fluoride. Place 40 c.c. of distilled water in the dialysis cylinder and 20 c.c. of blood in the fish-bladder condom (used as the dialyzer). The latter is hung in the water, so that the level of the blood is a few millimeters above that of the water. The cylinder is now closed with a cork, which at the same time catches and seals the neck of the condom. The apparatus is left at room temperature for two hours, when the water is drawn from the cylinder into an evaporating dish acidified with 6 to 10 drops of dilute hydrochloric acid. Again, 40 c.c. of distilled water are placed in the cylinder and the dialysis is allowed to continue two hours longer. The dialysate is drawn off, and the process repeated a third time. The 120 c.c. of dialysate in the evaporating dish are now carefully evaporated to dryness on a water bath and the murexide test is applied directly to the residue in the dish, as follows: A few drops of dilute nitric acid are placed in the dish and evaporated on a water-bath (not over the free flame). The dish is allowed to cool, several drops of ammonia are added, and again evaporated carefully. If uric acid is present, the residue in the dish is stained purplish red. On the addition of sodium or potassium hydrate, the color changes to reddish blue or violet. For quantitative determinations the method has not proved to be of value. The intensity of the murexide test is no index of the amount of uric acid present. The method is of value in the differential diagnosis of gout and certain forms of rheumatism, which resemble gout clinically. In about 200 gouty patients whose blood has been examined for uric acid quantitatively by the method of Krüger-Schmidt, it has been found that the blood is generally saturated with it (about 8.3 mg. of monosodium urate per 100 c.c. of blood).

SURGERY

UNDER THE CHARGE OF

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General Toxicity of Extracts of Hypertrophied Prostate.—LEGUEU and GAILLARDOT (*Jour. d'Urolog.*, 1912, ii, 1) have made a biological study of the problem of hypertrophied prostate by experimentation on dogs. These experiments were carried out by injecting a prepared substance containing material from the hypertrophied prostate of man in 10 experiments, from the hypertrophied prostate of the dog in 2, from a uterine fibroid in 1, and from an adenoma of the breast in 1, or with pathological tissues in 14. They were done with the normal prostate of the dog in 10, and the normal prostate of the horse in 2. There was a great difference in the toxicity of the various extracts employed. While with doses as large as 2 grams to the kilogram of animal weight, from the normal prostate of the dog as from the uterine fibroid or adenoma of the breast, no death occurred; on the contrary, in employing the pathological prostate of man, the animal was killed, twice with the dose of 1 gram to the kilogram, three times with the dose of 0 gr. 50, and seven times there were accidents more or less grave out of the 12 experiments. The normal prostate of the dog is less toxic for the dog than that of the horse, while the hypertrophied prostate of the dog is as toxic for the dog as the hypertrophied prostate of man, both being very toxic. Therefore, when a prostatectomy is done, a mechanical obstacle to the bladder is removed as well as something which has a local or general toxic effect on the patient.

Experimental Researches Concerning Ulcerations of Large Arteries from Contact with Drains.—WEISSENBACH and BERTIER (*Archiv. gén. d. Chir.*, 1912, vi, 754) say that the study of the ulceration of arteries, especially of large trunks, to their knowledge, has never before been combined with an experimental research. Humbert and Monod differ as to the cause of the condition. Monod believes in the inflammatory action and necrosing effect of the pus. Humbert attributes the important role to certain adjuvant conditions, particularly to drainage tubes too long maintained in the wound. The direct cause of this paper was a sudden, severe hemorrhage from the wound, following an operation for the removal of an adherent and inflamed appendix. The drainage tube was removed on the sixth day, when the patient was doing well, and two hours later the operator was

summoned hastily. Re-opening the wound was considered but was postponed because the hemorrhage had stopped and the patient was in a grave condition, dying soon afterward. The autopsy showed the pelvis and right iliac fossa filled with blood clots, and an opening in the external iliac artery at the site where the drainage tube pressed on it. Nine experiments, varying in details, were performed on dogs. By operating with strict asepsis in sound tissue and on a healthy artery, they were unable to produce ulceration of the vascular walls by simple contact of the drain or even with continuous and prolonged contact. If traumatic ulceration is possible from escharotic action or necrosis, it is only under very special conditions. The experimental work permitted the writers to emphasize the importance of the role of infection in the so-called traumatic ulcerations; the importance, no less great, of the role played by the drain as an agent for localizing the infection upon the artery, the rupture being only the mechanical consequence of the acute localization of the arteritis; and the necessity of intimate contact between the artery and the drain. Finally, from a practical point of view and so far as one can generalize for man, the experimental facts observed on the animal, these facts confirm what has been observed clinically. It is never necessary in the presence of infection, to permit a drain to remain in contact with an artery more than three days or even two days. If left longer, the mechanism outlined can provoke an ulceration of the vessel.

Surgical Treatment of Genital Tuberculosis in the Male.—Lapeyre (*Archiv. gén. d. Chir.*, 1912, vi, 774) says that the operative treatment of genital tuberculosis in the male has made an important advance, and that abstention is no longer the rule. Genital tuberculosis in the adult in its primitive form, is frequently a local, benign, and essentially surgical affection. In the absence of pulmonary and vesical tuberculosis, not only exposed but concealed foci in progressive evolution, should be operated on early. An operation passing beyond the lesion is the method of choice with two exceptions. One should try to preserve the testicle in 50 per cent. of the cases, and he should let alone prostato-vesicular lesions of mild grade, because they tend toward spontaneous cure. The operation of choice in the great majority of cases is vaso-epididymectomy, sufficiently but not excessively extensive. Resection of the sound vas deferens, in these cases, should be done systematically in order to save the second testicle (especially after loss of the first). Vaso-vesiculectomy, a rarer operation, should be done. It is of next importance to vaso-epididymectomy. The inguinal and perineal paths are clearly indicated. Bilateral castration should be done only in cases of absolute necessity. Extirpation of the whole genital tract, made grave by the removal of the prostate, is only an exceptional indication.

The After-treatment of Excision of the Knee with the Aid of Approximation of the Bones by a Screw Splint.—Kolb (*Zentralbl. f. Chir.*, 1912, xxxix, 812) says that the plaster cast, with or without a window in it, is employed by most surgeons. Kolb recommends an apparatus consisting of a metal splint made up of two pieces, one fitting and

sliding into the other and fixed at various lengths by a middle screw at each end. In the excision the bone surfaces are sawed straight and at right angles with the long axis of the bone. A hole is then bored in the lower end of the femur and one in the upper end of the tibia for the screws which are to fix the splint to the bones. The two pieces of the splint are made movable by loosening the middle screw, and are applied to the bones so that the holes in the ends are just over those in the bones, for the introduction of the screws. After these have been introduced and each splint piece has been screwed to the corresponding bone, the sawed surfaces of the two bones are pressed together in good position and the middle screw is made tight. The end screws are prevented from slipping in the holes of the splint by a small lateral screw for each. This permits the splint to be held away from the bones by the end screws, so that it remains 2 to 3 cm. above the skin surface. This renders the changing of dressings very easy. The limb is finally laid on a Volkmann's splint. In 4 out of 5 cases in which the method was employed, good bony union was obtained. In the fifth case amputation was later necessary, because of the general condition of the patient.

After-treatment of Excision of the Knee.—MERKENS (*Zentralbl. f. Chir.*, 1912, xxxix, 949) following Kocher, does away with all means of fixing the bone ends, aside from that furnished by the bandage. The end of the femur is sawed convexly, that of the tibia concavely. He advocates cleansing the joint cavity; division of the flexor tendons in children; adaptation of the bones; and the introduction of skin and fascial sutures. He believes ligation of the vessels is usually unnecessary, and, if possible, that no drainage should be used. While the bones are held in extension and closely together by a reliable assistant, the knee region is surrounded by a gauze-cotton dressing. The tourniquet is loosened. A plaster cast is then applied including the foot and the pelvis and extending to the umbilicus. The fixation is so good that on recovering from the narcosis the patients have no pain. If the cast presses anywhere this should be corrected. It is not removed for six to eight weeks when bony union is complete, and after removal of the skin sutures it is replaced by a lighter cast. If necessary to expose the wound a window can be made, although this will rarely be necessary. The good fixation and absence of suture material favors the primary union. Merkins regards the Kolb-Wilms apparatus as complicated.

The Technique and After-treatment of Excision of the Tuberculous Knee.—RIEDEL (*Zentralbl. f. Chir.*, 1912, xxxix, 1125) describes the operation which he calls a radical one. The transverse Volkmann incision extends to 1 to 2 cm. from the posterior surface of the knee on each side, and at each end is combined with a longitudinal incision extending about 6 cm. above and below. The sawing of the bones is begun with the limb extended to favor a correct position of the limb later, but is carried only to a depth of about 2 cm. The knee is now flexed for the first time and the sawing completed. After thoroughly cleansing away diseased tissue and ligation of all visible vessels, the

limb is elevated, and the tourniquet removed. After about fifteen minutes the limb is brought down and the patella which has been sawed transversely, is united by three thick catgut sutures passing around the bone. Then the transverse incision is sutured with catgut and the longitudinal wounds left open. No drainage is employed. An attendant on the operating table holds the limb vertically without traction on the foot. The sawed ends of the bones are fitted together and the knee is surrounded smoothly by one gauze layer after another, winding them firmly. Then follow the layers of gauze covering the limb above and below about 20 cm. from the wound. Upon the gauze are laid sterilized, very thin wooden splints (40 cm. long, 2 or 3 cm. wide, and 1.5 mm. thick) and more gauze is wound around them. When the bones are thus secured the attendant leaves the table and the limb is brought to the horizontal. A support is placed under the pelvis and the limb is covered with gauze, over these being placed long flexible wooden splints. Then the whole limb from the foot to the pelvis is wrapped in cotton in which is incorporated a thick wooden splint on the outer side. This is fixed as far as the waist by a bandage. Finally a Volkmann splint is applied to the knee. This dressing is allowed to remain in position six weeks, and at the end of that time it will be found almost always that union of the bones has taken place. The transverse wound is healed firmly, and at the site of the longitudinal wounds are strips of granulation tissue, which quickly heal over after removal of the granulations. Riedel emphasizes three details: (1) The sawing through the bones while they are in the horizontal position. A mild genuvalgum, more marked in women with their broader pelves than in men, is the normal position. (2) The first short bandage should be applied with the limb in the vertical position. (3) The dressing can be permitted to remain in position until union is complete because no foreign body (silk ligatures, drainage tubes) are left in. Riedel never employs a plaster cast.

The Technique and After-treatment of Excision of the Knee.—Kausch (*Zentralbl. f. Chir.*, 1912, xxxix, 1125) offers a contribution from his experience with excision of the knee, because his methods differ from the preceding in essential points. He observes the teaching of Mikulicz's clinic, making a transverse incision and sawing through the patella. Occasionally, he makes other incisions in order to follow and excise fistulæ. Like Riedel, he emphasizes the necessity of a radical procedure. He always saws the femoral condyle convexly and the tibia concavely. This curved sawing, while not easy, is not very difficult but requires a thin-bladed saw. Whenever possible, it should be so done as not to require correction, but when correction is necessary it can be done best by a large file with an even convex surface. The physiological valgus position should be preserved. It is not necessary that the sawed surfaces should be in exact apposition, nor does it do any harm if the removal of a focus leaves a hole or if there remains a defect in the intercondyloid fossa. The curved sawing usually permits the removal of the bone foci without taking away much bone, in consequence of which there is less shortening than when the sawing is done in a straight line. As a rule, the femur is more involved

by the disease than the tibia, and the outer surface of the bone more than the inner. Anteroposterior gliding is prevented by the curved surfaces of the ends of the bone and lateral gliding by the suturing of the patellar fragments with wire, after sawing from it a transverse piece corresponding in width with the shortening in the limb. Its posterior surface is also sawed off and the patella nailed to the lower end of the femur in order to keep the ligamentum patella tense. Drainage is employed only when there is severe mixed infection. A well padded posterior splint is applied, which extends from the buttocks to the heel. The limb is now brought down to the table without fear of dislocating the fragments. An anterior plaster and hemp splint is prepared which reaches from the toes to the inguinal region, and is applied firmly to the limb. The patient is returned to bed and the limb suspended by means of a ring in the anterior plaster-hemp splint. In the evening or at the end of twenty-four hours the plaster splint is removed and the rubber bandage, applied about the operative field to control oozing, is removed. The plaster splint is then replaced. The whole dressing remains in place for four to six weeks, when it and the skin sutures are removed.

Intravenous Administration of Sublimate, Hyrgolum, Oxycyanide, and Sublamine, in Salvarsan Relapses.—HEIDINGSFELD (*Amer. Jour. Urolog.*, 1912, viii, 434) says that despite the fact that salvarsan is the most efficient present day remedy for the successful treatment of syphilis, it does not possess, in itself, properties of unfailing efficacy. For a time he relied exclusively upon salvarsan to effect a cure, except in such cases as had received mercurials and other forms of antisyphilitic medication prior to the administration of salvarsan. The study of these cases reveals that many patients who had received some form of previous medication showed a negative complement fixation test of more prompt and permanent character than those who had received previous treatment of this kind. An effort was made to determine a more effective method of combining the mercurial with the salvarsan treatment. Intravenous administration of bichloride was made in 11 cases; of hyrgolum in 92; oxycyanide in 114; and sublamine in 15. Five cases progressed to an absolutely negative Wassermann under the intravenous administration of hyrgolum, 4 under the intravenous administration of oxycyanide, 6 under the influence of both ocycyanide and hyrgolum, and 1 under the influence of sublamine. Ten cases have shown material improvement and the rest remained unchanged, or have been observed too short a time to permit an estimation from the complement fixation standpoint. Sixteen cases, or 23 per cent. of the 69 cases which have failed to promptly become negative under salvarsan and mercurials in other form, have become Wassermann negative, and 10, or almost 15 per cent. have shown material improvement. These results are relatively low because many of these cases have been treated too short a time to determine the character of the Wassermann reaction. The writer feels sufficiently encouraged to recommend this method of treatment for further observation, study, and confirmation at the hands of others who are engaged in the treatment of these cases. He can only recom-

mend the oxycyanide of mercury when administered in dilutions of 1 to 1000, and in dosage not exceeding .02 gram. Great care should be exercised in its careful and proper administration. The vein must be carefully and properly entered without incision, to prevent disfigurement. Great care must be exercised not to produce an effusion of the remedy outside the vein. Such an accident while not immediately as painful as that of salvarsan, is prone to produce an inflammatory infiltration of rather severe and distressing character. A wider, more extensive experience and a more prolonged and careful observation, will determine to what extent it can be employed as a routine measure in the successful treatment of syphilis.

The Value of Direct Gastroduodenoscopy in Affections of the Stomach and the Duodenum.—Rovsing (*Annals of Surgery*, 1912, lvi, 201) ventures to assert that we have obtained in the direct gastroduodenoscopy described a method which, in those difficult cases where all other diagnostic expedients are insufficient, enables us to give the exact diagnosis in cases of disease in the stomach and duodenum. It is of special importance in three directions: (1) In the numerous cases where the symptoms speak in favor of ulcers, but where inspection and palpation of the stomach show nothing of the sort. Here gastroduodenoscopy removes all doubts, and sometimes shows us that the supposed ulcer does not exist, whereby the patient is spared a senseless and injurious encroachment; and sometimes it proves the presence of the ulcer, its seat, and its nature. (2) For the differential diagnosis between ulcers in the stomach and the duodenum. (3) By rendering possible a direct attack upon the ulcer, where one had formerly to content himself with gastro-enterostomy because the seat of the ulcer was unknown. This is of exceptional importance with ulcers, the hemorrhages from which constitute a menace to life whether there be permanent oozing, small bleedings, or violent, acute hemorrhages. Nor, naturally, is this method infallible; as with it also one may sometimes overlook a small ulcer which has concealed itself in the folds of the mucous membrane, and may sometimes interpret a depression as being the edge of an ulcer or something similar, but this is of rare occurrence.

THERAPEUTICS

UNDER THE CHARGE OF

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Luminal—A New Hypnotic.—Goldstein (*Deutsch. med. Woch.*, 1912, xxxviii, 987) believes that solutions of luminal are changed by boiling, and therefore the remedy is much less active when given subcutaneously.

The administration of the remedy by mouth is often impossible because of its intense bitter taste. He believes that the best effects are obtained when it is given in the form of suppositories. Thus in 79 per cent. of his cases sleep was induced when luminal was given by rectum, and in only 50 per cent. when it was given subcutaneously. Luminal acts slowly, according to Goldstein, requiring from one to two hours before sleep is produced. He believes that it is twice as active as veronal, but decidedly inferior to adalin as a sedative.

The Action of Salvarsan and Neosalvarsan on the Wassermann Reaction.—McDonagh (*British Med. Jour.*, June 8, 1912, p, 1287) gives his observations on the value of the Wassermann reaction as a guide to the treatment of syphilis. In the primary stage, when the reaction is negative before treatment is commenced, most cases give a positive reaction afterwards. This reaction is most marked about the forty-eighth hour. In some cases, on the other hand, the reaction does not become positive until the fifth day. Although it may remain positive for several days, the degree diminishes generally about the third week, until it becomes negative before the eighth week. If the reaction is only slightly positive after the injection, it becomes negative much earlier. If the first injection gives rise to only a weak reaction then three or four more will undoubtedly suffice to make the reaction permanently negative; if, however, the reaction is strong, then the patient is in the secondary stage, and will require at least 3 grams of salvarsan or neosalvarsan before the desired effect is obtained. In the secondary stage when the reaction becomes strongly positive after an injection, and in cases in which it is markedly positive before treatment is commenced, no blood tests need be made until before and after the fourth injection, as in McDonagh's experience the four injections are the minimum likely to be required to produce a permanent negative result. In the tertiary stage the Wassermann reaction behaves much in the same way as it does in the primary and secondary, except for one peculiar phenomenon, which is occasionally to be noted—that is, a case with a strong positive reaction before treatment may become negative immediately after an injection and remain so from twenty-four to seventy-two hours, and then becomes quite positive again. Patients who have had syphilis and give a negative Wassermann reaction are either cured or in the latent stage, which of the two can only be ascertained by giving a provocative injection of salvarsan and then testing the blood. As an injection of salvarsan will not give rise to a positive reaction in a non-syphilitic, one must regard the occurrence of such as indicative of the presence of disease, and efforts should be made to bring about a cure. Taking all stages of syphilis, McDonagh has found that three to seven injections are necessary to cure most cases of syphilis. There is no doubt that many cases in the tertiary stage can be cured with neosalvarsan which failed to be cured with salvarsan. Liable to change as these conclusions may be, he cannot but admit that the alterations in the Wassermann reaction as the result of treatment are most constant, and when tested at short intervals, give a much safer guide to regulate treatment than by saying that just so many injections will be required, or, as the old syphilologists used to teach, that a three years' pill treatment was

sufficient for all cases alike. As there is a possibility of fallacy, he advises his patients to have a provocative injection of neosalvarsan six months or a year after they have been discharged, and the blood tested forty-eight hours, the seventh, fourteenth, twenty-first, and twenty-eighth day after that injection.

Influence of Salvarsan Treatment on the Wassermann Reaction.—Müller (*Wien. klin. Woch.*, 1912, xxv, 873) notes the results of the Wassermann test in 85 cases of syphilis in the secondary stage treated with injections of salvarsan and observed for a considerable period of time after the treatment. The Wassermann test gave a negative response in from four to eight weeks after the injections in the majority of cases, but in more than half of these the reaction became positive again from three to twelve months later. In some cases the disease ran a malignant course with a constantly negative Wassermann reaction. One patient had been persistently treated for over two years with every known means of combating syphilis, but has never been free from manifestations of the disease for a single week, and yet the Wassermann test was always negative throughout. In another malignant case mercury proved ineffectual, but under salvarsan the manifestations of the syphilis temporarily subsided, while at the same time the previously constantly negative Wassermann findings became positive. The findings seem to indicate that although salvarsan has a more rapid therapeutic action on syphilis than mercury, yet it does not ensure a permanent cure.

Lumbar Puncture in the Treatment of Uremia.—Frey (*Correspond. Blatt. f. Schweiz. Aerzte*, 1912, xlii, 623) treated 8 of 20 cases of acute uremia by lumbar puncture and permanent benefit resulted in all but 2 cases in which the process was too far advanced to hope for even temporary benefit. In 1 case reported in detail repeated venesection had failed to relieve, but the beneficial effect of lumbar puncture was prompt and lasting. Frey believes that probably the effect of lumbar puncture is largely due to relief of mechanical pressure, although the removal of toxins may be an element. Frey notes that the symptom-complex of uremia is dependent upon many different factors. If the principle factor is retention by the kidneys, marked benefit will be derived from infusion. If the symptoms are largely dependent upon cardiac weakness, venesection will be of great value. It is in the type with marked cerebral symptoms that lumbar puncture will often be of great value toward saving life.

Clinical Experience with Luminal.—Loewe (*Deutsch. med. Woch.*, 1912, xxxviii, 947) says that luminal is a valuable sedative and hypnotic in all forms of insanity and also in excessive irritability and insomnia occurring in the course of neurasthenia. It is a very useful hypnotic when other hypnotics fail or are contraindicated. In cases of delirium such as delirium tremens, luminal exerts a sedative action in much smaller doses than are necessary with veronal. It is given as a hypnotic to normal individuals in doses of usually 0.2 gram and at the most 0.4 gram is necessary to secure physiological sleep. The remedy has been given in much higher doses in insanity without

apparent ill effects. Untoward effects such as fall in blood pressure intoxication symptoms, and habit formation are seen only in long-continued usage of the remedy, and are very similar to those produced by veronal. Luminal may be given by mouth in tablet form or the sodium salt of luminal which is easily soluble in water may be given in solution. The sodium salt may also be given by rectum, but it is especially valuable in that it may be given hypodermically. Loewe says that the combination of small doses of morphine with luminal is as effectual as hyoscin except its action is not so prompt.

The Salvarsan Treatment of Pernicious Anemia.—BRAMWELL (*British. Med. Jour.*, June 22, 1912, p. 1413) adds to a previous communication in which he reported 2 cases of pernicious anemia much benefited by the administration of salvarsan. These 2 patients have remained apparently well for over a year without any further treatment. He reports 5 other cases treated on the same plan. One of these 7 cases showed very striking improvement, four injections of 0.3 gram each being given during a period of six weeks during which time the red blood cells increased from 1,760,000 to 3,350,000 and the hemoglobin rose from 52 per cent. to 78 per cent. During the year following the last injection the blood continued to improve steadily, the red blood cells increasing to 6,210,000 and the hemoglobin rising to 120 per cent. Five other patients showed more or less improvement, and in only 1 of the 7 no benefit whatever was derived from the treatment. Bramwell believes that the beneficial effects were definitely dependent upon the salvarsan and not a coincident. He is of the opinion that salvarsan is a more efficient remedy than arsenic given by mouth. To secure the best results salvarsan should be given intramuscularly, on account of the prolonged action which results from its slow absorption when so given.

The Treatment of Scarlet Fever with Salvarsan.—KLEMPERER and WOITA (*Therapie d. Gegenwart.*, 1912, liii, 198) relate their experiences with the salvarsan treatment of a series of 39 cases of scarlet fever of severe type. They compare the results they obtained with cases occurring in the same epidemic treated by the usual symptomatic method. They were led to try this method of treatment because of the curative action of salvarsan in many diseases, not closely related. Among these may be mentioned a group of infections caused by some variety of spirillum, another group caused by animal parasites, and again a number of diseases of entirely unknown origin. Another factor which led them to try salvarsan was that the Wassermann reaction has been found positive in severe types of scarlet fever. Of the 39 cases treated with salvarsan, 5 died, a mortality of 12.6 per cent. as compared with 24.5 per cent. mortality in 44 cases not treated with salvarsan. The percentage of complications was also much smaller in the cases treated with salvarsan. Thus otitis media developed in only 6.6 per cent., as compared with 14.3 per cent. in the untreated cases; nephritis occurred in 25 per cent. as against 43 per cent.; and endocarditis was observed in 3 per cent. instead of 16 per cent. The therapeutic effect of the remedy was marked upon the course of the disease, especially upon

the temperature. In all but 2 cases the temperature fell by crisis shortly after the injection. This fall was followed by a rise on the following day, but seldom to the original height of the fever. A few of the patients received a second injection of salvarsan. The doses given were 0.1 to 0.2 gram to infants, 0.3 gram to older children, and 0.5 gram to adults. Most of the injections were given intravenously and only were given in highly diluted form intramuscularly when intravenous injections were impossible. Klemperer and Woita hope that further experience will confirm their belief in the value of salvarsan in the treatment of scarlet fever.

PEDIATRICS

UNDER THE CHARGE OF

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Vaccines in the Treatment of Pertussis.—MAYNARD LADD (*Archives of Pediatrics*, 1912, xxix, 581) reports the results of vaccines prepared from Bordet's bacillus on cases of pertussis. Bordet's bacillus, while not universally recognized, is fairly well established as the causative factor in pertussis. It is a small cocco-bacillus found in the expectoration from the paroxysmal cough of pertussis; it can be grown on serum or blood-bouillon and gives the agglutination and complement test for pertussis. Vaccines from this bacillus were used on selected cases of typical pertussis, the blood counts showing a relative increase in the mononuclear cells. A minimum interval of five days was allowed between injections, but the intervals were often increased to two weeks, as the cases were not brought to the hospital regularly. There were no general or local reactions from the injections, and as many as 40,000,000 bacteria were given as one dose to children aged nine months, and were repeated several times without bad effect. No other treatment but the vaccine was given. All the children recovered without complications on an average in five weeks after beginning the injections. On an average the cases were in the third week of the disease when the treatment was started. The usual, long drawn out course lasting from two to three months was absent. It is believed that by using larger doses at shorter intervals a greater efficiency of the vaccines may be established.

Intestinal Poisoning under the Guise of a Cerebral Affection.—OSWALD MEYER (*Deutsch. med. Woch.*, 1912, xxxviii, 1550) calls attention to that class of intestinal toxemias occurring in children aged under three years in which the cerebral symptoms hide the true condition and made a correct diagnosis difficult. Many cases of the cerebral type would be saved if the intestinal condition were sus-

pected, and adequate treatment given for it. He describes one case as an example in which the child became suddenly ill with fever, vomiting, convulsions, coma, athetoid movements, and spasticity of the left arm, loss of patellar and pupillary reflex, spasticity of the left side, and conjugate deviation of the eyeballs. The condition continued four days, improving, however, when purgation and colonic irrigation were employed because offensive stools suggested intestinal poisoning. The coma and loss of reflexes persisted for four days, clearing up slowly. The urine was negative. The child recovered under the treatment for intestinal poisoning, and in nine days was well. Conjugate deviation is usually found only in true cerebral conditions, although one-sided convulsions and spasticity may occur in intestinal poisoning. The cerebral localization suggested by the one-sided symptoms can only be explained by a general diffuse irritation of the centres, which had more effect upon certain motor centres than upon others. Meyer mentions a second case in which the long duration of the cerebral symptoms could only be explained by the severe symptoms of intestinal poisoning, the foul odor of the stools persevering for four days even after the cleaning out of the bowel. One should not neglect this possibility of intestinal poisoning in cerebral cases and should not employ chloral too soon or too freely until the intestinal tract is thoroughly cleaned out. If the interval between the onset and the clearing of the bowel be too long the symptoms will continue until the poisons get out of the blood stream. To facilitate the latter the use of normal saline solution is advised.

Massage in Wasting Diseases of Children.—J. M. MacPhail (*British Jour. Child. Dis.*, 1912, ix, 404) reports excellent results in infants with wasting diseases by employing general massage. He holds that wasted babies, particularly in infirmaries and institutions, do not thrive better because they lie inertly most of the time and are not nursed and handled, thereby missing a general manipulation essential to muscular and vascular tone. He describes his results with children in the wards of a hospital. These children were rubbed routinely with codliver oil, but, as many of them did badly, he instituted general massage lasting half an hour, and stretching out all the muscles. He also employed the Schäfer and Sylvester methods of artificial respiration to promote better circulation and prevent stagnation in the lungs. The general and local conditions speedily improved, the muscles became firm, and the children ate and slept better. In one case, a baby aged seven months, wasted from a chronic diarrhea, gained 4 pounds 2 ounces in twelve weeks, and improved markedly. Another case of marked rickets with intestinal catarrh in a baby aged ten months, gained 4 pounds 1 ounce in seven weeks, and showed marked improvement. All the cases were improved by this treatment. Both of the cases cited above gained without any alteration in diet.

The Treatment of Asthma in Children.—H. E. Knopf (*Berlin. klin. Woch.*, 1912, xlix, 1566) reports 5 cases of asthma in children, all of them cured and with no return of the disease so far. Asthma is found in children more frequently than is commonly believed. The import-

ant part of the treatment lies in teaching the patient to use his muscles of respiration properly. In asthma the thorax attempts inspiration at the same time that the abdomen attempts expiration. All complications of asthma, excepting the nervous forms, are benefited and often cured by this method of treatment. Other therapeutic measures are naturally not neglected, especially the supervision of the child's food, especial stress being laid on having only milk and vegetables for supper and having them eaten early so that the stomach is empty at bedtime. Attention to the child's environment and hygiene are important factors in treatment, and it is advisable that the child be given sanatorium treatment for a short time for its psychic effect. It appears that asthma, like stuttering, sometimes disappears at puberty. The treatment includes psychical influence, development, change of environment, and the teaching of normal breathing by daily breathing gymnastics.

Typhoid Fever in Infancy.—J. P. Crozer Griffith (*Archives of Pediatrics*, 1912, xxix, 565) gives an analysis of 75 cases of typhoid fever in infants aged two and one-half years and under. The duration of the onset in 44 cases was not over seven days in 58 per cent., and not over five days in 28 per cent. In some cases the onset lasted only two or three days. It was sudden in 35 per cent. and rapid in 27 per cent. of the cases, illustrating the tendency to rapid onset in children. Fever rose rapidly, reaching its height much sooner than in adult life. There is a much greater tendency to diarrhea during the onset in children than in early or later childhood, and this symptom was present in 57 per cent. in this series. Vomiting occurred as an early symptom in 34 per cent. of the cases. Headache was noted in 14 cases, all aged at least two years. Cough was infrequent at the onset, being noted in only 18 cases. Epistaxis is significant by its absence, being noted in but 4 cases. Tympanitis is infrequent at the onset. Abdominal pain or tenderness was noted in but 12 cases. Convulsions were noted in but 3 cases, showing the striking absence of this sign. The symptoms of the developed attack show many digestive signs. Coated tongue is common, anorexia infrequent, and abdominal distention, and bronchitis common. Nervous symptoms are not marked, and the typhoid state exceptional. The course of the fever is not characteristic, being steadily high or moderate, and later often irregular, but it may be irregular from the beginning. The fall is often rapid. The total duration of fever is three weeks or less in most of the cases. Typhoid roseola is common, appears early, from the fourth to the sixth day, and was present in 48 cases. The spleen was enlarged in one-half of the cases. The Widal reaction is characteristic, as in adults. Leukocytosis is absent. The urine often shows albumin and casts. Complications occurred in 31 cases and consisted of exanthemata, 1 intestinal hemorrhage, and 25 per cent. of suppurative processes, the last being a tendency in infancy. Relapses occurred in 3 cases. The type of the cases was rather severe, the mortality being 12 or 16 per cent. The treatment was symptomatic. Tubbing, with the water at 90° or 100° F. is preferred to sponging. The diet was largely milk, including cereal gruels, broth, and beef juice.

OBSTETRICS

UNDER THE CHARGE OF

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Uterine Scar after Cesarean Section.—HARRAR (*Amer. Jour. Obstetrics*, May, 1912) contributes an interesting paper upon uterine scar after Cesarean section, by giving the experience of the Lying-In Charity of New York. He reports 3 instances of vaginal delivery in patients who had previously had abdominal Cesarean section, describes the gross appearance of the scar in repeated sections, and reports cases of rupture of the uterus, 4 in number, after one or more sections. Microscopic studies were made of the scar in cases of rupture, and in those cases where rupture had not occurred. He concludes that in undertaking Cesarean section on a patient who has been long in labor, with ruptured membranes, and who may be infected, we must recognize the probability of obtaining a poorly healed scar which would make future pregnancy dangerous. In repeated Cesarean section it is best to excise the old uterine scar rather than make a new incision parallel to it, thus avoiding the isolation of a weakened strip of uterine wall between two scars. In the after-treatment of Cesarean section, should lochia be retained, intrauterine douches should not be given because of the danger of infection and mechanical injury to the uterine wound. In managing a case where Cesarean section has been previously performed for the relative indication, one must be guided by the history of the previous convalescence, as well as by the method of suture employed. We must thus estimate the integrity of the old scar and its capacity to endure the strain of vaginal delivery. The microscopic study, in cases where rupture had occurred, showed that in some patients the normal uterine muscle had not developed in the scar, but had been replaced by attenuated connective tissue, which readily gave way. In other cases rupture occurred through uterine muscle the nutrition of which had been impaired by the adjacent scar.

Rupture of the Cranial Dura Mater in the Newborn.—MEYER and HAUCH of Copenhagen (*Archiv. mensuelles l'Obstétrique*, March, 1912) report 28 cases of rupture of the cranial dura mater in the newborn occurring in 1200 confinements. In 13 this rupture and hemorrhage were considered the cause of death; 6 of these were still-born, and 7 born living. In 4 cases the child was very large and was extracted by a difficult forceps operation. In 1 case the birth was accomplished by difficult breech extraction. In all, death was the result of this accident in 12 cases in 1200 confinements, or 1 in 100. Hemorrhage is greatest where the rupture is at the tentorium, as there the vessels are most abundant. Rupture through the falx cerebri does not cause great bleeding, and in no case was serious injury observed in the inferior longitudinal sinus. Where the two layers of dura mater

have completely ruptured, hemorrhage is abundant, and the child is still-born. In some instances a large vein is torn across. This accident occurs in spontaneous labor where expulsion occurs very rapidly. In one case the child died from ulcer of the stomach, probably due to hemorrhage some days after delivery. In 10 cases breech extraction produced the accident; in 1 case difficult forceps extraction. Comparison shows that this rupture occurs more often when the child is extracted by the feet and breech than when delivered by forceps.

Prognosis of Repeated Classic Cesarean Section.—MAIROTON (*Archiv. mensuelles l'Obstétrique*, March, 1912) reports 38 cases of repeated Cesarean section in the Tarnier clinic at Paris. It was found that where the first operation had been done under aseptic precautions, with a correct suture, the risk of rupture in the scar in subsequent labor was not sufficient to cause hesitation in performing section. In the repeated operation, in 7 cases there were adhesions which complicated somewhat the second procedure. In 2 there were adhesions between the uterus and omentum, and in 2 between the uterus and the abdominal wall. There seemed to be no difference in the various sorts of suture material provided they were sterile and properly introduced. Infection is a great cause for adhesions, but this may be so mild as to produce few if any symptoms. Adherence of the membranes to the uterine wall renders delivery more easy; hemorrhage was not observed. It was thought best to excise the old scar at the following operation. In making the repeated section, the operator must be careful in opening the abdomen to avoid the coils of intestine which may be adherent to the abdominal wall. At repeated operation, the question of sterilizartion must be decided by the circumstances present with each patient. Abortion does not occur as a result of this operation, and a premature labor rarely happens. In 19 cases the patient came into spontaneous labor at term, or was operated upon at term, just before the commencement of labor. In one patient in whom a third operation was done, the uterus was adherent to the surrounding tissues. Mairoton concludes from his experience that the repeated operation is justifiable.

Retroversion of the Gravid Uterus with Over-distention of the Bladder, and Hematuria.—BARRIS (*Jour. of Obst. and Gynec. of British Empire*, April, 1912) reports the case of a multipara about four months pregnant, who had severe pain in the lower part of the abdomen, and great difficulty in emptying the urinary bladder. As some urine was discharged, and the patient objected to the use of the catheter, it was not employed. The patient continued to suffer with pain in the bladder region and could only pass urine with difficulty. The abdomen increased in size and the legs became swollen. On admission to hospital the abdomen was greatly distended by a tense elastic tumor, reaching within an inch of the border of the ribs. Seven pints of clear urine were withdrawn by catheter. Three and one-half hours afterward, three and one-half pints were withdrawn. On examination the uterus was found pregnant, about three months, lying above the pelvic brim, and extending into the abdomen. It had previously

been displaced by the fingers, the first examination having found the uterus in the hollow of the sacrum. The subsequent treatment of the case consisted in catheterization every four hours and the administration of urotropin. Examination of the urine showed the presence of red blood corpuscles with alkaline reaction. Microörganisms were absent. A rubber ring was worn for some time until the uterus was sufficiently large to remain above the pelvis, and the urine had become normal. The patient's pregnancy went on normally.

Cesarean Section for Dystocia, Due to Coils of the Cord around the Fetus.—Briggs (*Jour. of Obst. and Gynec. of British Empire*, April, 1912) reports the case of a multipara in labor, the fetal head lying transversely above the brim, with the occiput to the right. Labor had been in progress ten and one-half hours, but the cervix admitted one finger only. On the following day the membranes ruptured prematurely, with half dilatation. Progress ceased, and the patient's pains were quieted by morphine. On examination, a short cord was diagnosticated as the cause of delay, and as mother and child were in good condition, delivery was effected by Cesarean section. The fetus weighed 8 pounds, 2 ounces; the cord measured 28 inches in length, and was coiled tightly about the fetal neck. The placenta was implanted on the anterior right wall of the uterus, and in delivering the child a large area of the placenta and its short portion of intact cord were withdrawn. The pallor of the child was threatening at first, but the child was resuscitated when the cord was loosened.

Congenital Graves' Disease, and Total Occlusion of the Duodenum in the Newborn.—White (*Jour. of Obst. and Gynec. of the British Empire*, April, 1912) reports the birth of a fetus in the first labor of a mother who suffered during pregnancy with characteristic exophthalmic goitre. The child was delivered by forceps, weighing 4 pounds, 6 ounces. It presented the characteristic features of Graves' disease, with exophthalmos and tremor of the hands. The thyroid was enlarged, the heart action very rapid, and a loud murmur was heard over the precordium. The child remained deeply cyanosed. It lived thirty-five hours only. The mother improved, but in a subsequent pregnancy her symptoms again became worse, and she gave birth to a stillborn, premature child, without abnormality. An examination of the body of the fetus showed a large subdural hemorrhage over the right parietal region, extending over the temporosphenoidal lobe. The suprarenals were large, the thyroid enlarged, and an accessory thyroid was found under the root of the tongue. The thyroid substance, on examination, was sterile. Microscopic examination of the thyroid showed proliferation of cells, with colloid material. The second case was that of a normal, and normally-sized male infant born in spontaneous labor from a healthy multipara. At birth there was a large umbilical hernia, whose sac covering burst, exposing the intestine. The lower end of the bowel reached the abdominal cavity through an aperture immediately above the umbilicus, causing sufficient compression to produce congestion in the intestine. The hernia was too large to permit of its reduction by operation. Beginning peritonitis was present. The child took nourishment for some hours,

but later vomited a large quantity of fluid. The meconium was white in color, and a diagnosis of congenital obliteration of the bile ducts was made. The child had seemed to be in constant pain, which was not subdued by morphine. Death occurred after thirty-six hours. On postmortem examination the duodenum ended in a cul-de-sac lined with normal mucous membrane. There was nothing to indicate where the jejunum was attached, but on the outer coat of the blind extremity was a solid cord continuing into the small intestine, of the usual size. The occlusion was not near the neck of the hernial sac. The whole intestine was filled with white cheesy material containing no trace of bile.

GYNECOLOGY

UNDER THE CHARGE OF

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Kidney Changes Following Sudden Occlusion of the Ureter.—In view of the varied and often diametrically opposite statements as to just what happens to the kidney after occlusion of the ureter, which are to be found in the standard text-books, and of the by no means infrequent occurrence of injury to the ureter during gynecological operations, several studies of the subject from the experimental and clinical standpoint, which have recently been reported, are of interest. KAWASOYE (*Zeitschr. f. gyn. Urologie*, 1912, iii, 172), whose investigations as to the best method of permanently occluding the ureter, when it is desired to do this, have already been reviewed in these pages, has examined the kidneys in a series of 10 rabbits killed from two to seventy days after the ligation of one ureter. He found a hydronephrosis of the corresponding kidney in every instance, this being greater in amount the longer the time which had elapsed between the operation and the death of the animal. Up to the fourteenth day he found an increase in the weight of the parenchyma, due to retained urine in the tubules; after this time atrophy occurs. The chief microscopic changes noted were hyperemia, dilatation, and atrophy of the tubules; complete disintegration of the entire parenchyma did not occur in any of his experiments, but he believes that that would doubtless have been the end result, had any of the animals been permitted to live long enough. In a similar series of experiments, where the ureter was loosely tied, but not completely occluded, no hydronephrosis was produced, merely a marked dilatation of the ureter above the point of ligation. A third series of experiments was undertaken to ascertain how long a ureter can remain completely occluded without the kidney losing its integrity. It was found that if the ureteral obstruction is removed in from two to four days, the kidney undergoes complete functional regeneration, as judged by the indigo-carmine test; partial regeneration may take place up to one or two

weeks, but after three weeks no secreting power whatever could be demonstrated. Quite similar experiments have been performed on 30 dogs by SCOTT (*Surg., Gyn. and Obstet.*, 1912, xv, 296). In some of these he produced a permanent, in others an intermittent obstruction, by ligating the ureter with a rubber band, tight enough to produce complete obstruction until the pressure in the pelvis of the kidney became sufficient to stretch the rubber band and let the fluid escape. He also found that complete obstruction to the ureter always causes hydronephrosis, the degree depending upon the duration of the obstruction; intermittent obstruction has the same effect, but does not act so quickly. He found the chief changes in the parenchyma to be dilatation, first of the straight tubules, then of the convoluted tubules, and lastly of the glomeruli. His experience has been that in even the highest degree of hydronephrosis the kidney epithelium is never entirely destroyed, but is capable of further secretion; in only one of his cases of incomplete, and in no case of complete obstruction, did atrophy of the kidney occur. A study of the same subject, from the clinical as well as the experimental side, is reported by BARNEY (*Surg., Gyn., and Obstet.*, 1912, xv, 290). He has collected from the literature and by personal communication 62 cases of sudden and complete ligation of the ureter by ligature or clamp, most of these having occurred during a vaginal or abdominal hysterectomy. In 46 of these cases the occlusion was unilateral, in 16 bilateral. In 20 per cent. of the former, no symptoms whatever, either immediate or remote, were noticed, the patients making a complete and uneventful recovery. In but 1 case of unilateral obstruction did anuria and death follow. This agrees with Barney's experimental results, unilateral ligation of the ureter in 26 dogs and 7 rabbits failing in a single instance to produce this renorenal reflex. In 26 per cent. of the cases of unilateral obstruction observed clinically there was some transient pain or tenderness in the kidney region, but only in one instance was this so persistent as to necessitate a subsequent nephrectomy. In no case of bilateral ligation was any pain produced. Barney believes that where pain is produced this is probably the result of intense renal congestion, with stasis of urine; owing to the formation of anastomosing vessels, providing new channels for the venous circulation, this congestion gradually subsides, and the pain is relieved. In 24 per cent. of the clinical cases, urinary fistulæ established themselves, an occurrence which was never noted in the experimental work. In 15 per cent. of the unilateral ligations, infection of the corresponding kidney followed, but this was never seen in the bilateral cases. Experimentally, Barney also has found that ligation of one ureter is practically always followed by the development of hydronephrosis. In only 15 of the clinical cases was the subsequent condition of the kidney noted, but in 12 of these hydronephrosis was present. In most of them the obstruction was relieved before many days had elapsed, so that no large sacs were encountered. In one instance the obstruction was not released until ten days after the operation, but then the kidney took up its normal function, apparently unimpaired; the same was true of several others in which the occlusion has lasted from five to six days. From these facts, and the results of experimental work, Barney concludes that after the release of a ureter long obstructed, the kidney usually displays

remarkable recuperative power; an organ which at first appears of little value may prove an important factor in the elimination of metabolic waste, so that unless a kidney under these circumstances is definitely proved worthless, nephrectomy should not be hastily performed.

Operation for Carcinoma of the Vulva.—STOECKEL (*Zentralbl. f. Gyn.*, 1912, xxxvi, 1102) calls attention to the almost uniformly bad results that are obtained in the surgical treatment of vulvar carcinoma, and to the lack of any serious efforts to improve them, comparable to those which have been expended on carcinoma of the cervix. He believes that these bad results are due chiefly to the very early metastases caused by this form of carcinoma in the regional and more distant lymph glands, together with the age and poor general condition of many of the patients. The glands principally affected are the inguinal, iliac, and hypogastric. Although the latter can be reached extraperitoneally by a pararectal incision, Stoeckel prefers to approach them transperitoneally after opening the abdomen in the midline, as this permits of a better view and more thorough extirpation. Having removed as thoroughly as possilbe all the pelvic glands, the laparotomy wound is closed, and two long oblique incisions are made, starting at each anterior superior spine, and meeting in an obtuse angle over the mons veneris. Through these the inguinal glands with their surrounding tissue are removed in one mass, care being taken to clean out the triangle between the sartorius and pectineus down to the fascia and vessels. This accomplished, the next step is to make a vertical incision from the mons veneris downward, passing around the vulva, and then to shell out the entire vulvovaginal tissue, keeping close to the anterior surface of the symphysis and the internal edge of the pubic arch. Only after complete freeing of the vagina from the urethra, from the pubic bone, and from the rectum, is the tumor mass finally cut away. All wounds are closed with fairly free drainage, and a permanent catheter is placed in the bladder. Stoeckel believes that if every case of vulvar carcinoma, in which there is the slightest chance of radical extirpation, were subjected to this operation, carried out under spinal anesthseia, the percentage of permanent cures would be much higher than it is at present.

Trauma as a Factor in Rupture of Pyosalpinx.—Three interesting cases of the rupture of a pyosalpinx, in which the immediate cause appeared to be a single acute trauma, are reported by JAWORSKI (*Gyn. Rundschau*, 1912, vi, 478). The first case was that of a woman, aged thirty-six years. Several workmen were carrying a piano out of her house, and appeared to be letting it fall, when the patient sprang forward and made a violent effort to help lift it. She immediately fell to the ground in a faint; in a half hour vomiting set in, accompanied by clammy sweat. In a few hours she died, and at autopsy both tubes were found transformed into pus sacs, the left one containing an area of rupture the size of a dollar. Death was due to acute peritonitis. The second patient was aged forty years. On the third day of a menstrual period she was seized with sudden, lancinating pain in the lower abdomen immediately after lifting a heavy wash-tub.

She fell unconscious; this was followed in her case also by vomiting and collapse. Death occurred the same night. At autopsy an area of rupture the size of a bean was found on the anterior wall of a left pyosalpinx, accompanied by an acute pelvic peritonitis. The third patient was aged forty-two years. She was seized during the act of coitus, performed during the menstrual period, with lancinating pains, followed by violent vomiting, and died on the following day. At autopsy bilateral pyosalpinx was found, with acute peritonitis. In the mid portion of the right tube was an opening from which thick, yellowish pus was discharged. In all these cases the rupture occurred after physical exertion, which was accompanied by increased abdominal pressure. In 2 menstrual congestion seems to have played some role, and Jaworski believes that the congestion attendant upon coitus may also be at times an important factor. The extreme gravity of rupture of an acute pyosalpinx is well illustrated by these 3 cases, in every one of which the patient died inside of twenty-four hours. In one case operation was advised, and refused, but in the others the condition of the patient was so desperate from the start that operative interference could not be considered.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Carcinoma of the Tongue Treated by Adrenalin.—Holscher reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 7 Livraison, 1912) a case of carcinoma of the tongue, the size of a hen's egg, which had necessitated tracheotomy. He commences by injecting a few drops of adrenalin, gradually increasing to 2 grams a day. As a result, the tumor began to undergo gangrene and to be thrown off in part. At the moment of presentation there existed only a very small tumor at the base of the tongue.

Farcy (Glanders) of the Larynx and Pharynx.—Mahu reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) a case of pharyngolaryngeal farcy in a veterinary surgeon, aged thirty years, whom he had treated for two months for grave ulcerations of the larynx and pharynx in sequence to an infection of glanders beginning with pleuropneumonia, followed by abscesses localized in the anterior portions of the limb and the adductors of the thigh. All treatments, topical and general, had been without result. Poyet had occasion to see a case of laryngotracheal farcy in a veterinarian. He found the larynx ulcerated at its anterior portion with invasion of the arytenoids, and ulceration of the anterior portion of the trachea. At the autopsy an uninterrupted ulceration was seen

to extend from the larynx to the bifurcation of the trachea, with a perforating ulcer at that point which had been the immediate cause of death.

Asphyxia from Descent of Excised Adenoids in the Trachea, Revealed by Bronchoscopic Intervention.—GUISEZ, in a recent paper read at the French Congress of Otology, Rhinology, and Laryngology (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912), upon the escape of adenoid vegetations in the air passages, reported several cases of his own observation. In 3 of them the presence of the vegetations was revealed by bronchopulmonary manifestations, which in 2 instances ensued after emesis and ejection of the vegetations at the end of ten to fifteen days. In another case the offending body was removed under bronchoscopic intervention. Finally, quite recently, Guisez had been called to an infant in a paroxysm of asphyxia from which it was freed by the removal of a mass of vegetations which straddled the bronchial spur.

A New Method of Plastic Injections.—BRÜNINGS (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911) describes a new method to supersede paraffin injections in saddleback noses and similar deformities by substituting fat tissue taken from the body of the individual. One advantage is that the fat remains in position without shifting, as the paraffin sometimes does.

Radical and Aseptic Cure of Frontal Sinusitis by Plugging the Sinuses.—TORRINI describes (*Revue Hebd. de Lar., d'Otol. et du Rhinologie*, December 9, 1911) a new radical procedure for the cure of frontal sinusitis, avoiding the disfigurement produced by other methods. He raises the periosteum, destroys the anterior wall of the sinus, curettes the interior, enlarges the infundibulum, and then plugs the cavity with the lead paste of Beck, replacing the periosteum.

Nasal Stenoses.—For the prevention of nasal synechia, MOURE (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) interposes very thin sterilized plates of mica to avoid or correct postoperative nasal synechia. Its suppleness and its flexibility permits it to be readily insinuated between the raw surfaces, and it thus forms a thin partition which does not present the inconvenience of a foreign body, nor produce any secretion or granulation, and cicatrization is thus facilitated on both sides.

A New Treatment for Paralysis of the Recurrent Nerve.—BRÜNINGS claims (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911) to overcome the effects of the paralysis by stiffening the paralyzed vocal band artificially with hard paraffin injections. This he usually accomplishes in two sittings. In the first one he injects the middle, anterior, and posterior portions of the vocal band about midway of its transverse surface. Five to eight days later the intermediate portions of the vocal band are injected. In this way he succeeds in converting the flaccid vocal band into a stiffened structure in permanent position for phonation.

Facial Paralysis following the Use of the Nasal Douche.—Lebut-Barbon reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 7 Livraison, 1912) a case of a man, aged thirty-nine years, who was in the habit of washing his nose every day for nasal catarrh. On one occasion this produced intense pain in the left ear, followed four or five days afterward by a facial paralysis which existed for six weeks and gradually subsided spontaneously.

Laryngeal Paralysis as the First Symptom of a Cancer at the Base of the Skull.—Mahu reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) this case in a very robust man, aged fifty-four years, and a great smoker, who consulted him for aphonia, pain in the temporomaxillary region, and a left recurrent paralysis, with very slight cervical adenitis. Eight days later inequality of pupils suggested neoplasm at the base of the brain, then tumefaction occurred rapidly, and finally an ulceration at the vault of the pharynx, with purulent discharge and invasion of the left nasal fossa and maxillary sinus. The recurrent paralysis had existed only fifteen days. The patient died cachectic at the end of four months after ineffective treatment with radiotherapy.

Secondary Cancer of the Larynx.—Secondary cancer of the larynx is very rare. A case has been reported by Lannois and Montcharmont (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) in which the patient succumbed two days after his entry to the hospital where he had been admitted with the diagnosis of cancer of the larynx at the level of the right arytenoid and the right aryteno-epiglottic fold. At the autopsy there was in addition, an epithelioma of the ectodermic type in the middle portion of the esophagus. Other cases on record have been traced as true metastases in cancer of the breast, of the rectum, and of the skin.

Gastroscopy.—In a demonstration on gastroscopy before the German Laryngological Association (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911), Elsner exhibited a gastroscope with an optical cystoscopic attachment which enables him to inspect the interior of the entire stomach within two or three minutes.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Pneumococcus Infection in Man and Animals.—Wadsworth (*Jour. Exp. Med.*, xvi, No. 1, July, 1912) publishes two interesting papers

giving results of experimentation directed to the possibility of a cure of pneumococcus infection. The author considers that we may liken lobar pneumonia in man directly to pneumococcus infection in animals. A rabbit is extremely susceptible, with production of a general systemic infection from which recovery may occur by crisis; the dog, on the other hand, tends to show local tissue reaction due to the fact that its protective mechanism is powerful, so that although there be characteristic lung lesions, crisis does not occur. Wadsworth is inclined to think that it is the bacteriemia rather than the lung lesion which accounts for many of the manifestations of the disease seen in man. The extensive lesion is an expression of the efficiency of the protective mechanism of the body, with the result that infectious agents in such lesions may actually disappear. Extensive lesions, however, are due at their inception to virulent pneumococci, and this virulence is a necessity before the systemic manifestations can occur. Immune sera are well known to vary greatly in their curative value, although this does not necessarily mean that their protective action is slight. When animals are actively immunized, their immunity to culture filtrates is very definite, but injections with dead culture material are by no means so efficient as injections with virulent living cultures. In rabbits, treatment with such serum induces crisis and cure, but although virulent pneumococci show little reaction in the test-tube to a given serum, nevertheless subsequent infection by the special organism is an exception to the general rule. The pneumococcus toxins are presumably active only in the body tissues, and manifestations of the disease arise from this action. Immune sera can neutralize these poisons and terminate the symptoms of the disease, the pneumococci remaining as parasites to be destroyed in the ordinary course of events. This immunization may occur quickly and completely as in crisis, or in contrary manner, as in lysis. By analogy, Wadsworth considers that sera from animals highly immunized with living cultures of virulent organisms ought to cure the disease.

Hemoglobinemia and Hemoglobinuria.—Pearce, Austin, and Eisenbrey (*Jour. Exp. Med.*, September, 1912, xvi, No. 3) give details of experiments with normal and splenectomized animals with regard to the excretion of hemoglobin. They find that there is a "threshold value" for the kidneys by which, when a concentration of 0.06 grams of hemoglobin per kilo of body weight is reached, the hemoglobin appears in the urine. The amount of hemoglobin per kilo of body weight which may exist without excess of bile pigments appearing in the urine, is about 0.22 grams, and this marks the "threshold value" of hemoglobin for the liver, although it is pointed out that the more slowly the hemoglobin is injected, the less likelihood is there of the appearance of choluria. When a relatively large amount of hemoglobin is injected intravenously, hemoglobinuria appears in a very few minutes; if a relatively small quantity be injected rapidly, it may appear with choluria; even moderately large amounts slowly injected may be eliminated without the occurrence of choluria. The absence of the spleen does not appear to affect the elimination of hemoglobin by the kidneys. Pearce, Austin and Eisenbrey's idea is

that hemoglobinuria does not occur until hemoglobinemia reaches the level of 0.06 gram per kilo body weight. When this amount is surpassed hemoglobinuria occurs, and when the concentration is less than this it ceases. The liver, however, and perhaps other tissues, take up hemoglobin as soon as it appears in the serum, and deal with it regardless of its excretion by the urine. The kidneys remove 17 to 36 per cent., and the liver takes the rest to be transformed into bile pigment. If the circulation be flooded with a large amount of hemoglobin absorbed rapidly, the bile pigments cannot be rapidly enough removed, and reabsorption into the blood occurs with the appearance of choluria. Pearce, Austin, and Eisenbrey would thus explain those cases in which hemolysis is accompanied by jaundice without hemoglobinuria; the liver removes the hemoglobin so rapidly that the minimum necessary for hemoglobinuria is not reached. Nevertheless, even under these circumstances a liver may absorb a large amount of hemoglobin so that bile formation is so excessive that jaundice appears. As a corollary to this, a very large amount of hemoglobin appears quickly in the urine until the excess has been removed, when it no longer appears, the slow elimination of the remainder by the liver causing the subsequent choluria. Experiments by Pearce, Austin, and Krumbharr with regard to splenectomy leads them to suppose that the spleen is essential for the breaking up of hemoglobin, or for the building up of its derivatives, and that there is an interrelation between the spleen and the blood-forming organisms, as well as between the spleen and other blood-disintegrating organisms. The bile-forming function of the liver is disturbed by splenectomy so that in the first four weeks after the operation, hemoglobinuria was not followed by jaundice, while after a period of three and a half months jaundice occasionally occurs, apparently indicating a rehabilitation of the function of the liver.

Salvarsan and Sublimate.—An account was recently given (*Jour. de Phys. et Path.*, July 15, 1912, xiv, No. 4) in which MOREL, MOURIQUAND, and POLICARD have made a comparison between the effects of toxic doses of salvarsan and of bichloride of mercury. Salvarsan has, relatively, a slight effect upon the kidney and a relatively marked effect upon the liver; about three times as much arsenic will lodge in the hepatic cells as will be found in the renal epithelium. As is well known, bichloride of mercury attacks the kidney with great avidity, so that the organ is rapidly damaged; on the contrary, its action upon the liver is relatively slow and slight, the action in each case bearing a direct relationship to the amount of the drug. It may be recalled that Oettinger and Fiessinger were enabled to examine a case of poisoning by intramuscular injection of mercury, and to discover 0.01 centigram of mercury for each 1000 gram of liver tissue, while three times as much was found per 1000 grams of kidney tissue.

The Distribution of Iodine in Normal and in Syphilitic Tissue.—The researches of O. LOEB (*Archiv. f. Exp. Path.*, 1912, lxix, 108) upon this subject support the belief that when iodid of potash is absorbed in health it does not remain in any demonstrable quantity in the

brain, the fat, or the bone marrow. It can be found in the liver, kidneys, lungs, the blood, and the thyroid glands. Disease in these and other tissues alters their adaptability to retain iodine, so that tuberculous or carcinomatous tissue contains more iodine than the same tissue in health. Secreting glands which are diseased by syphilis contain from three to six times as much as normal blood, and the less severe the syphilis, the greater the readiness of the tissue to hold iodine. In such tissues the iodine is in an organic combination, presumably an iodine and albumin compound being formed. It has doubtless been a puzzle to every reader to understand the action of so-called "alteratives;" it is, however, in tissue irritated by a virulent agent that these show their best powers, due perhaps to the readiness with which iodine forms (soluble?) combinations in such tissues. Certain it is that at times gummas or other proliferations of endothelial tissue seem to melt away under the action of iodine.

The Parasitology of Trypanosomiasis.—WOLBACH and BINGER (*Jour. of Med. Research*, September, 1912) have investigated the histological changes observed in trypanosomiasis. While their results show nothing remarkably new, they have examined with much care, the lesions set up by the presence of trypanosomes. As has been previously shown, these are decidedly of the nature of connective-tissue reaction to an irritant of low virulence. The essential change is proliferation of endothelial cells, and the activity of these cells, resulting from the presence of the parasites, causes the increase of large mononuclear cells which can be observed in the blood. Following the invasion of the tissue, there may be edema, there is constantly cell proliferation, fibrosis, and infiltration by plasma cells. The endothelial cells may block the vessels and undergo hyaline degeneration, after which fibrosis is seen to occur with occasional giant-cell formation. Granular leukocytes are conspicuously absent in the lesions, and when the parasites are engulfed it is in almost every case by the endothelial cells. Although lesions are to be found everywhere, the connective tissue structures are especially prone to be the seat of change, a case parallel to the changes observed in syphilis, although it must be noted that the trypanosome has little power to invade the skin. Wolbach and Binger have been able to observe the parasites setting up lesions in the central nervous system. From all the lesions observed, Wolbach and Binger deduce a very low degree of toxicity in the parasites, and the form of parasite which they consider most active in producing lesions in the flagellate.

The Disinfection of Drinking Water by Chlorinated Lime.—ANTONOWSKY (*Zeitschr. f. Hyg. u. Infekt.*, 1912, lxxii, Heft 3) investigated the possibilities of disinfecting water for drinking purposes by minimal amounts of chlorinated lime, and found that the method was a good adjuvant to the usual mechanical means. The efficient agent in the chemical is the acid, and a certain duration of time to allow its action is essential; if the time allowed be too short, the bacteria are not killed; and in the experiments in which the destruction of bacteria was incomplete, the virulence of those organisms that remained was

not affected in the slightest degree. The action of chlorinated lime can be nullified by the presence of sodium hypochlorite, and assisted by the presence of katalysing substances.

The Experimentally Alcoholic Heart and Liver.—Bischoff (*Zeitschr. f. Hyg. u. Infekt.*, 1912, lxxii, Heft 3) in dealing once more with this much-studied question, places the cardiac change in the most prominent place; true it is that central grouping of the fat occurs in the liver, but in rabbits the heart muscle changes are by far the more important. The site of predilection for the intracellular deposit of fat Bischoff states to be under the epicardium of the left ventricle toward the apex, as well as in the papillary muscles; the outer lamellæ of the right ventricle are also liable. The kidneys were not found to be markedly affected. The fat content measured from the dried substance of the heart showed in rabbits fed with alcohol a rise from 11 to 12 per cent; lecithin-content showed a considerable decrease, both absolute and relative; lecithin, which was nearly 60 per cent. of the total fat-content in the normal, became only 37 per cent. in the alcohol-fed animal, with a corresponding lessening in amount of cholesterin.

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All communications should be addressed to—

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